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Original Communications

FETAL RESPIRATION IN RELATION TO ATELECTASIS AND INTRAUTERINE PNEUMONIA*

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(From The Johns Hopkins University)

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THE PATIENT AND THE WEATHER. By William F. Peterson, M.D. Vol. IV. Part 3. Organic Disease—Surgical Problems. Edwards Brothers, Inc., Ann Arbor, Mich, 1938.

HEMORRHOIDS. By Marion C. Pruitt, M.D., Atlanta, Georgia. President, American Proctologic Society, Associate in Surgery, Emory University School of Medicine, etc. With 73 illustrations, including 7 in color, 170 pages. The C. V. Mosby Company, St. Louis, 1938.

SYMPTOMS OF VISCERAL DISEASE. A Study of the Vegetative Nervous System in Its Relationship to Clinical Medicine. By Francis Marion Pottenger, M.D., Medical Director, Pottenger Sanatorium for Diseases of the Chest; Professor of Clinical Medicine, University of Southern California, etc. Fifth edition, with 87 text illustrations and 10 color plates, 442 pages. The C. V. Mosby Company, St. Louis, 1938.

ESSENTIALS OF OBSTETRICAL AND GYNECOLOGICAL PATHOLOGY, with Clinical Correlations. By Marion Douglass, M.D., Assistant Professor of Gynecology, Western Reserve University, and Robert L. Faulkner, Senior Clinical Instructor in Gynecology, Western Reserve University. With 148 illustrations, 187 pages. The C. V. Mosby Company, St. Louis, 1938.

SEX SATISFACTION AND HAPPY MARRIAGE. By the Reverend Alfred Henry Tyrer, Clergyman of the Protestant Episcopal (Anglican) Church. Foreword by Robert L. Dickinson, M.D., New York. Emerson Books, Inc., New York, 1938.

EAT AND KEEP FIT. Scientific Secrets of Diet. By Jacob Buckstein, M.D., Consulting Physician in Disease of the Stomach to Central Islip Hospital, etc. 128 pages. Emerson Books, Inc., New York, 1938.

TEXTBOOK OF CLINICAL PATHOLOGY. Edited by Roy R. Kracke, M.D., Professor of Pathology, Bacteriology and Laboratory Diagnosis, Emory University, etc. With the assistance of twelve outstanding contributors. Illustrated, 567 pages. William Wood & Company Division, Williams & Wilkins Company, Baltimore, 1938.

EL CICLO DE LA MUCOSA VAGINAL EN LA MUJER. Par Guillermo di Paola. Illustrated, 76 pages. Editor: El Ateneo, Buenos Aires, 1938.

THE ADRENAL CORTEX AND INTERSEXUALITY. By L. R. Broster, Clifford Allen, H. W. C. Vines, Jocelyn Patterson, Alan W. Greenwood, G. F. Marrian and G. C. Butler. With a foreword by Sir Walter Langdon-Brown. Illustrated, 245 pages. Chapman & Hall, Lim. London, 1938.

ANNUAL REPORT ON THE RESULTS OF RADIOTHERAPY IN CANCER OF THE CERVIX. First volume, collated in 1936. With appended Atlas. Edited by J. Heyman, Stockholm. Health Section of League of Nations. Geneva, 1937.

THE SINGLE WOMAN AND HER EMOTIONAL PROBLEMS. By Laura Hutton, physician, Tavistock Clinic, London. Second edition, 173 pages. William Wood and Co., Baltimore, 1937.

LEÇONS DU JEUDI SOIR A LA CLINIQUE TARNIER. Publiées sous la direction de A. Brindeau. Un volume, 318 pages, 66 figures. Vigot Frères, Paris, 1938.

LIÇÕES DE CLINICA OBSTETRICA. Par Clovis Correa da Costa, chefe do Serviço de Ginecologia do Hospital da Fundação Gaffrée-Guinle. Livraria Moura, Rio de Janeiro. 1938.

PROGRESSIVE RELAXATION. By Edmund Jacobson, A.M., Ph.D., M.D., Laboratory for Clinical Physiology, Chicago. 494 pages. The University of Chicago Press, Chicago, 1938.

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sult that an animal was available in which fetuses within the uterus could be observed at full term, or at stages of postmaturity corresponding in development to newborn rabbits of one, two, or three days.

In the course of the experiments various anesthetics were used in order to permit exposure of the uterus. Occasionally, as the depth of anesthesia was diminished, a few irregular respiratory movements of the fetuses were noticed. These gasps tended to confuse the results of the experiments with stimulant drugs. It was decided to eliminate general anesthetic agents entirely. Accordingly, section of the lumbar spinal cord was done to produce loss of sensation over the abdominal region to be incised for laparotomy.

The first experiment carried out with this new technique, namely, the inhibition of labor and the elimination of anesthetics, disclosed the errors of experimental methods heretofore used, and revealed the intrauterine origin of respiration (Snyder and Rosenfeld, 1937).¹

Fetuses within the uterus were breathing actively. Rhythmical excursions of the chest wall and diaphragm continued throughout periods of observation lasting many hours. Through the thin uterine wall of the rabbit we could distinguish unmistakably that the movements were respiratory. Similar findings were obtained in the cat and guinea pig.

Observations were next made upon women. Spontaneous fetal movements of regular rhythm and of a distinctive pattern characteristic of fetal respiration were seen to be transmitted through the abdominal wall, and motion picture records of them were obtained (Snyder and Rosenfeld, 1937).²

Up to the present time asphyxia of the newborn has been approached by the clinician and the physiologist from a standpoint which has regarded the problem to be a matter of the sudden initiation of activity in a previously dormant system. In recent years the solution of the problem has been sought in terms of possible causes of the first breath of the newborn (Barcroft);³ search has been directed toward discovery of some mechanism which suddenly comes into operation at the time of birth.

Recognition of the origin of respiratory movements early in embryonic life necessitates revision of previous views. Inquiry must be directed to the determination of factors which may arrest activity rather than to those which might initiate a new process. With regard to the causes of intrauterine respiratory failure it may be pointed out that in rabbit fetuses showing regular respiratory movements, apnea may be induced of three different types, namely, (1) anoxemic; (2) acapnic; (3) anesthetic.

Prevention of asphyxia of the newborn, therefore, centers in the period preceding birth. It involves the recognition and control of factors which cause fetal anoxemia, and suggests caution in the selection and dosage of anesthetic and hypnotic agents.

Certain anatomic abnormalities of the lungs which are observed at the time of birth, namely, atelectasis and pneumonia, may be traced to pathologic complications of normal intrauterine respiration. The entrance of amniotic fluid into the alveoli of the lung is not a pathologic complication of labor, but can be clearly demonstrated to be a normal

consequence of fetal respiration. The presence within the lung of amniotic fluid and a tidal exchange of this fluid between the alveoli and the amniotic sac has been proved by experiment. India ink injected into the amniotic sacs of littermates enters the alveoli or the lungs of fetuses which are breathing, but in apneic fetuses fails to enter the lungs (Snyder and Rosenfeld).⁴

The rate of exchange of fluid between the lungs and the amniotic sac has also been determined. In breathing fetuses particles of ink enter the lungs within a minute after injection, blackening of the lungs being easily evident without magnification.

Additional evidence showing that the alveoli contain amniotic fluid before birth is afforded by the regular occurrence of cellular debris of amniotic fluid in the lungs.

In the light of these findings it is evident that breathing of abnormal amniotic fluid containing debris of excessive amount or abnormal type may result in injury of the lungs before birth. Obstruction of bronchioles during intrauterine life may lead to incomplete dilatation of alveoli, or atelectasis. Contamination of the amniotic fluid by irritant substances, e.g. meconium, or bacteria may cause inflammatory changes of the lungs before birth, and result in the death of the fetus with intrauterine pneumonia.

The occurrence of fetal respiratory movements throughout a large part of intrauterine life and the effectiveness of these movements in maintaining a tidal flow of amniotic fluid between the interior of the lungs and the amniotic sac lead to the conclusion that intrauterine respiratory movements are essential for the development of a normal lung.

II. DILATATION OF THE PULMONARY ALVEOLI BEFORE AND AFTER BIRTH

In order to compare the state of dilatation of the alveoli in lungs obtained before air is breathed with those of animals which had breathed air for various intervals following delivery, rabbits were prepared according to the method previously described for the observation of intrauterine respiration. Fetuses were removed from one horn of the uterus and after breathing of air for periods of one minute or longer, the trachea was clamped. The animal was dropped into formalin. A half-hour later the chest wall was incised to facilitate fixation; two days later the lungs were removed for histologic examination. As a control, fetuses of the opposite horn were dropped into formalin without removal from the uterus, after the trachea had been clamped through the intact uterine wall. Intrauterine respiration was occurring in many of these fetuses at the moment when the clamp was applied.

Results of a typical experiment are illustrated by lungs obtained from three littermates, sacrificed at twenty-nine days, which is the beginning of the period of viability. In the control fetus which had never breathed air, the lung is not collapsed but the alveoli are patent and well developed (Fig. 1). The degree of dilatation of the alveoli reveals the influence of intrauterine respiratory movements.

With the onset of breathing of air there is a striking increase in the dilatation of the alveoli which is clearly evident within one minute following delivery (Fig. 2). In a littermate which survived delivery for two days, the dilatation of the alveoli is increased still further.

Investigation has also been extended to the human being to include observations upon the structure of the lungs before and after birth. In human fetuses obtained before the breathing of air, the lungs were not completely collapsed but showed well-formed alveoli (Fig. 3). It was definitely known that no air had been breathed, since the full-term fetus was obtained at autopsy, being removed from an intact amniotic sac two hours following death of the mother from eclampsia. The cervix was not dilated and the membranes were unruptured. The alveoli are patent and the degree of dilatation reveals the effectiveness of the tidal movements of fluid throughout the respiratory tract. It is evident that respiratory movements within the uterus exhibit a function which is retained throughout postnatal life, namely, the capacity to expand the alveoli.

Microscopic examination of the human fetal lung gives additional evidence that the alveoli are not empty before birth but that amniotic

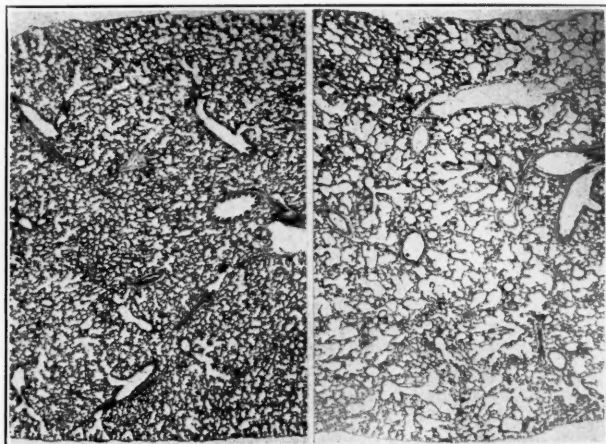


Fig. 1.

Fig. 2.

Fig. 1.—Normal rabbit lung before birth. The fetus was showing regular respiratory movements within the uterus at the time of sacrifice. $\times 20$.

Fig. 2.—Increase in size of the alveoli one minute after delivery and the onset of the breathing of air. The animal is a littermate of the fetus in Fig. 1. The rapid expansion of alveoli at birth prevents drowning of the newborn. The alveolar surface now obstructed by amniotic fluid thus becomes relatively greatly reduced. $\times 20$.

fluid fills the lung (Fig. 4). Cells and debris, characteristic of amniotic fluid are readily identified in the alveoli and bronchi of fetuses which had died before removal from the amniotic sac.

Another problem arises at this point. If the alveoli are filled with amniotic fluid at the time of birth, why is the newborn not drowned? A clue is afforded by microscopic examination of the lungs shortly after delivery when breathing of air has just begun.

In the lung of a child which had died eight and one-half hours after delivery (Fig. 6), the dilatation of the alveoli is in striking contrast to that observed in lungs obtained before the breathing of air had begun (Fig. 5). In the human being, as well as in the rabbit, it is

evident that, although the lungs contain amniotic fluid at the time of birth, the elasticity of the alveolar walls permits an increase in size of the alveoli of such magnitude that the surface area now obstructed by fluid becomes relatively greatly reduced.

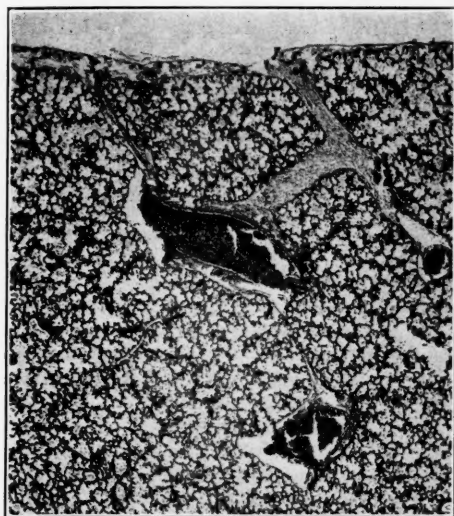


Fig. 3.—Normal human lung before birth. The alveoli are not collapsed, but are distended with amniotic fluid as a result of intrauterine respiratory movements. No air was breathed, since the full-term fetus was removed at autopsy from the intact amniotic sac, two hours following death of the mother from eclampsia. $\times 20$.

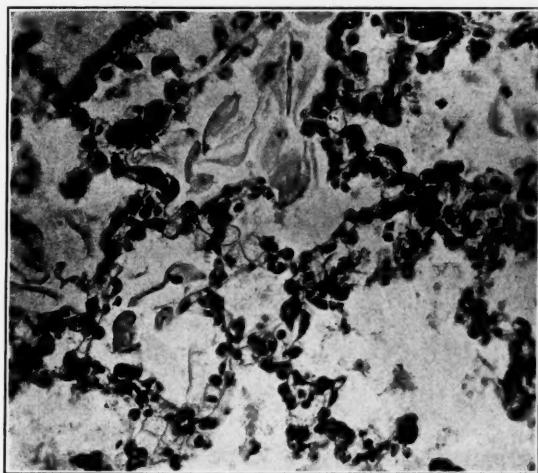


Fig. 4.—Alveoli of normal human lung before birth containing cellular debris of amniotic fluid. Same section as Fig. 3. $\times 350$.

In brief, a comparison of the structure of the lungs before and after birth shows that there is a gradual preparation for the sudden transition at birth from placental to pulmonary ventilation. Two stages in the expansion of the alveoli are clearly revealed: in the first stage, occurring

during intrauterine life the alveolar septa become thin and the alveoli are partly dilated; in the second stage, occurring after the breathing of air, there is a rapid increase in alveolar expansion. Current views regarding atelectasis of the newborn and its pathogenesis have been reviewed and criticized recently by Farber and Wilson (1933).^{5, 6}

The foregoing attempt to determine the normal degree of dilatation of the alveoli during intrauterine life on the one hand, and on the other to distinguish that stage of expansion which characterizes early postnatal life, may clarify the nature of atelectasis. It seems evident that atelectasis may arise during intrauterine life as a consequence of obstruction of the normal tidal flow of amniotic fluid in the respiratory tract. In case obstruction occurs at the time of delivery, there will be failure of alveolar expansion beyond the stage normally present within the uterus. In establishing criteria for the recognition of atelectasis during early postnatal life it may be pointed out that the increase

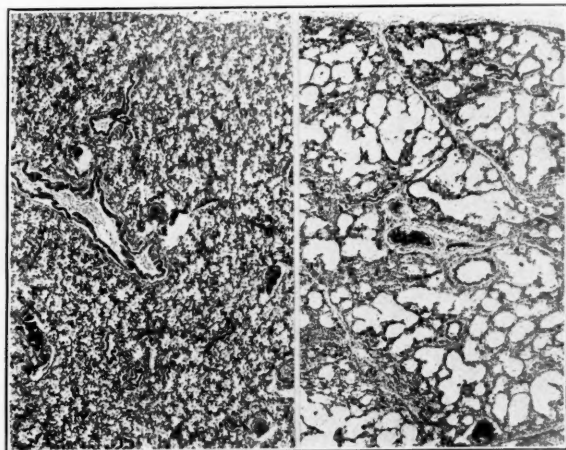


Fig. 5.

Fig. 6.

Fig. 5.—Lung of child before the breathing of air. The alveoli are well formed, showing that respiratory movements serve to expand the alveoli before birth as well as afterwards. The baby was stillborn following obstruction of the umbilical circulation during labor at term. $\times 20$.

Fig. 6.—Lung of child after breathing of air for eight and one-half hours, showing great increase in size of the alveoli. The baby cried at once following delivery by forceps at term but respiration ceased eight and one-half hours later. Autopsy showed intracranial hemorrhage and rupture of the tentorium. $\times 20$.

in expansion following the breathing of air is not uniform throughout all of the alveoli (Fig. 6). Widely dilated alveoli are seen adjacent to areas in which expansion of alveoli has not yet exceeded the stage characteristic of intrauterine life.

CONCLUSIONS

1. The lungs are not collapsed before birth, but the alveoli are well formed and partly dilated, being filled with amniotic fluid.
2. Breathing of air instead of fluid results in a rapid increase in the dilatation of the alveoli.

3. The newborn is not drowned although the lungs are filled with amniotic fluid at the time of birth. Adequate aeration is promptly provided, since the elasticity of the alveolar walls permits an increase in size of the alveoli of such magnitude that the surface area now obstructed by fluid becomes relatively greatly reduced.

4. Breathing of abnormal amniotic fluid containing debris which obstructs the respiratory passages may result in injury of the lungs before birth and cause atelectasis. Bacterial contamination of amniotic fluid may result in intrauterine pneumonia.

REFERENCES

- (1) *Snyder, F. F., and Rosenfeld, M.*: *Am. J. Physiol.* **119**: 153, 1937. (2) *Idem*: *J. A. M. A.* **108**: 1946, 1937. (3) *Barcroft, J.*: *Lancet* **2**: 647, 1935. (4) *Snyder, F. F., and Rosenfeld, M.*: *Proc. Soc. Exper. Biol. & Med.* **36**: 45, 1937. (5) *Farber, S., and Wilson, J. L.*: *Am. J. Dis. Child.* **46**: 572, 1933. (6) *Idem*: *Ibid.* **46**: 590, 1933.

DISCUSSION

DR. RALPH M. TYSON.—Dr. Snyder has shown us that the respiratory system functions before birth. Our problem as obstetricians and pediatricians is now to assist this system to carry on while the great changes in environment are occurring. Heretofore we have been accustomed to regard the problem simply as one of helping to initiate respiratory function after birth has occurred.

In a study of deaths over a seven-year period, we have found that early placental separation, placenta previa, abnormal cord conditions, and unknown causes of asphyxia, caused 14.4 per cent of the total deaths. If we were to add the deaths caused by cerebral trauma and atelectasis, newborn deaths due to asphyxia would reach 20 per cent. In addition many newborn babies recover from asphyxia, the cause of which in many instances is only a guess. These figures give a small idea of how important is this problem of respiration in the newborn.

Neonatal statistics are not of much help as given at present. The international list groups too many conditions under the heading "other diseases peculiar to early infancy." Asphyxia deserves separate mention and some steps should be taken to secure more detailed information on the part it plays in newborn mortality. A commission similar to the one on maternal mortality might be a good way to help solve this important problem.

DR. HENRY S. RUTH.—Since Dr. Snyder has mentioned the depressing action of certain anesthetic and analgesic drugs I would like to compare their characteristics which affect the maternal respiratory function, and therefore the respiratory activity in the newborn.

In the accompanying table I have listed only the agents commonly employed namely ethyl ether, chloroform, divinyl ether, cyclopropane and nitrous oxide. The characteristics about which we have definite information have been graded for each of these various agents on a sliding scale, 5 being the maximum response, and 1 the minimal response.

The most important information we should know about an agent is in regard to its depressing action on respiratory function. All the inhalation agents, with the exception of cyclopropane, produce a primary stimulation with a subsequent depression of respiration in the deeper stages of anesthesia. With ether and chloroform, on-coming depression occurs at the lower level of the second plane of the third stage of anesthesia. Cyclopropane, of course, is more depressing than ethyl ether, but its depressant effect is overcome to a large extent by the large volume of oxygen with which it is administered. Neither nitrous oxide or ethylene are in themselves depressing to respirations, but when accompanied by varying degrees of oxygen deprivation, corresponding degrees of respiratory depression are present. The duration of this depression of respiration is to a certain extent proportional to the elimination time of the agent. Ethyl ether and chloroform are eliminated

slowly; cyclopropane more rapidly, and ethylene and nitrous oxide more quickly than the other three. The elimination time, of course, is graded as it exists under average conditions, for with any given anesthetic it will vary with both the length of time and the depth of administration.

TABLE I. ACTION OF CERTAIN ANESTHETICS AND ANALGESICS

SCALE OF VALUES ++++ +++ ++ + 0	DEPRESSING EFFECT ON RESPIRATION	ELIMINATION TIME	O ₂ CONTENT AVERAGE CONDITIONS	POTENCY WITHOUT O ₂ WANT	EARLY RESPIRA- TORY STIMULATING EFFECT	CO ₂ CONTENT OF BLOOD	PRELIMINARY SEDATIVES	
							NON-VOLATILE AGENTS (THERAPEUTIC DOSES)	DEPRESSION RESPIRATORY CENTER
(C ₂ H ₂) ₂ O*	+++	+++++	++	+++++	+++++	-	Morphine sulphate	+++++
CHCL ₃ *	+++++	+++++	++	+++++	+	+++++	Barbiturates	+ to +++
(C ₂ H ₅) ₂ O*	+++	++	++	+++++	+++++	-	Scopolamine	0
C ₂ H ₄ †	+ or ++†	++	+ or ++	++	++	+ to +++	Atropine	Stimu- lating
C ₃ H ₈ §	+++++	+++	+++++	+++++	0	+++++		
N ₂ O†	0†	+	+	+	++	+ to +++		

*Open drop method administration.

†Semiclosed method administration.

‡Without sustained anoxemia.

§Closed c.c. absorption.

The oxygen content of the absorbed mixture under average conditions is somewhat dependent on the method of administration. With ether, chloroform, and ethyl chloride, when administered by the open drop method, some of the oxygen in the air will be displaced by the vapor of the anesthetic. Consequently, the customary 20 per cent is thereby somewhat reduced. The mucus produced by the irritant action of these agents also interferes with absorption which further decreases the intake of oxygen. With nitrous oxide and ethylene, the oxygen content of inspired mixtures is likely to be further decreased because of the relatively feeble nature of these agents. With cyclopropane the oxygen content is, of course, very high, as already explained.

The carbon dioxide content of the maternal blood has a relationship to the probable necessity of resuscitating the newborn. With an agent that markedly stimulates respiratory function, and with no provision for re-breathing, the carbon dioxide will, to a large extent, be eliminated. This occurs with ethyl ether and divinyl ether. Chloroform is a definite depressant to respiration, and therefore the carbon dioxide content of the blood will be high. With nitrous oxide and oxygen, the CO₂ of the blood depends largely on the amount of re-breathing instituted. With cyclopropane, which has no early respiratory stimulating effect, the carbon dioxide content of the blood is believed to be at a high level.

Among the nonvolatile sedative agents morphine sulphate has of course the greatest respiratory depressing effect. The barbiturates may be graded from 1 to 3. Scopolamine stimulates metabolism, and therefore the respiratory center, but this action is counteracted by its cortical depressant quality allaying emotional activity. Atropine stimulates the respiratory center to a certain slight extent, and probably also affects respiration directly through the mechanism of stimulating metabolism.

From the above description we learn that nitrous oxide is well adapted to obstetric anesthesia and analgesia if sufficient oxygen can be administered with it. Continuous care is, however, indicated to prevent anoxemia and anoxia. Cyclopropane is a depressant, but its elimination time is rapid and the high oxygen content administered with it is favorable. Ethyl ether is not quite so favorable, largely because of its slow elimination time.

I would like to ask Dr. Snyder about the results of spinal anesthesia on intra-uterine respiratory movements and more about his experience with the barbiturates. I would like to ask how long he believes the intrauterine respiratory movements may be abolished by either anoxemia or anesthetic action, and still allow the fetus to be delivered viable.

Finally, since it has been our clinical impression that when cyclopropane has been administered for longer than fifteen to twenty minutes before delivery, there may be some difficulty in resuscitating the baby. I should like to know whether Dr. Snyder has administered it for more than fifteen minutes, and if so, whether or not there was ultimately produced an absence of these intrauterine respiratory movements.

DR. PENDLETON TOMPKINS.—We know that the total alveolar surface of the lungs is very large, and now Dr. Snyder has shown that before birth the alveoli are filled with amniotic fluid. It is therefore quite possible that an important fluid exchange, through transudation, occurs in the fetal lung. If such transudation can be shown to occur we may be able to explain certain cases of hydramnios or oligohydramnios. It is noteworthy that oligohydramnios has been noted in association with congenital stenosis of the trachea. Is this oligohydramnios the result of interference with fluid exchange through the lower respiratory tract?

DR. SNYDER (closing).—To explain the asphyxia associated with cesarean section under local anesthesia, or following spinal anesthesia, one might speculate as follows: Of the three types of fetal respiratory failure which were observed experimentally, namely, anesthetic, acapnic, anoxemic, one can rule out the first and second, leaving only anoxemia to be considered. The oxygen supply of the fetus may be diminished by impairment of the uterine circulation resulting from increased tonus of the uterine muscle. This effect becomes more marked as term is approached, since at this time the uterus responds more readily to stimuli, like exposure to air in the course of cesarean section, spinal anesthesia, oxytocic drugs.

Dr. Ruth asked how long after the circulation has been interrupted is it possible for a fetus to be born alive. We have done the following experiment. The entire litter of a rabbit at full term was obtained within the unopened uterus after sacrifice of the maternal animal and prompt extirpation of the intact reproductive tract. At various intervals fetuses were removed from the uterus and their ability to survive was noted. If removal to the air was delayed longer than fifteen minutes, the animals did not survive. Injury may be evident much sooner, and they may start to breathe but eventually succumb. Obviously this simple experiment does not settle the matter in the case of the human being.

With regard to the duration of narcosis in relation to the condition of the fetus at delivery, a large problem is presented. The matter of dosage arises and quantitative studies become necessary. We have merely tried to illustrate the qualitative aspect, namely, that the effect upon the fetus may differ strikingly from that upon the mother, following administration of numerous anesthetic and hypnotic agents. With cyclopropane the mother was deeply anesthetized, showing no corneal reflex for fifteen minutes at least, and yet the fetuses were breathing at a rapid, uniform rate. The opposite was true with pentobarbital, for with this drug fetal respiration was depressed or abolished before the maternal animal gave evidence of analgesia. Obviously, the fetus has a special physiology.

In connection with the question of the absorption of amniotic fluid by the fetal lung and the relation of hydramnios to fetal respiration, it is interesting to note that amniotic fluid is greatly reduced invariably in the rabbit as term is approached.

Regarding the removal of debris from the upper respiratory tract in resuscitation, one may stop to reconsider how much fluid the child can tolerate in the respiratory tract. The baby seems to have greater resources in taking care of fluid than we had surmised. Of course, amniotic fluid differs widely among individuals with respect to the amount and type of debris. One child is covered with a thick vernix caseosa while another is clean. Injury of the fetal lung results from breathing of abnormal amniotic fluid.

VISCERAL ALLERGY

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ALLERGY is a new science with unlimited possibilities. It may be of interest to abstract the first paragraph of a previous article to convey a broader concept of this difficult subject. The local and general manifestations of allergy are due to a local or general hypersensitivity to certain provocative substances, allergens, which either gain entry into the circulation by absorption through the alimentary tract, or by bacterial invasion, or by hypodermic injections; or they may act locally by contact, inhalation or any other mode of approach. The presence of an allergen either in the circulation, or by contact, in sensitive individuals, produces in the sensitive tissues certain protective antibodies, or antigens, which are liberated by these cells when the allergen invades their domain, and the resultant is a form of irritation expressed either as an extravasation or a spasm. The extravasation is due to definite changes in the capillary lining epithelium, and the spasm, it is thought, is due to irritation of the neuromuscular mechanism. These antibodies are called allergins. They are a protective device. The results in the sentient patient are protean in their symptomatology. The cells or organ affected determine, to a great extent, the nature of the symptoms. In the nose, the common manifestation is hay fever, or hemorrhages due to plasma, or cellular extravasations, respectively; asthma, due to involuntary muscular spasm and extravasations; urticaria, due to focal skin dystrophies; local edemas, due to subcutaneous outpourings; eczema and prurigo, due to disturbance of nerve nutrition; and disturbances of the genital cycles, due to spasm or derangement of the normal secretions. These are the commonly recognized manifestations. But there is no organ or system of the body which may not be the seat of allergic symptoms. It was shown, in a previous work, that the sex organs are commonly affected; that the migraine is an expression of brain allergy, and cases of spreading paralysis and coma were quoted, of undoubted allergic origin.

It is proposed to detail the cases in which unusual and startling trains of symptoms arise out of involvement of specific organs in allergic states, producing conditions closely simulating the well-recognized organic diseases. These will be dealt with in the following order: Intestinal, hepatic, peritoneal, cardiac, muscular, and cerebral.

Intestinal Allergy.—In a paper entitled "Mucous Colitis"¹ Goodall named allergy as one of the frequent causes of colitis. Further observation has confirmed this opinion beyond refutation. The condition may be a more or less permanent, chronic state, or it may be periodic in its

manifestations, just as allergic states, as described and accentuated in a previous paper on allergy of the pelvis.² It may be added that the symptoms may be fixed in one part of the bowel, or may shift, affecting now one section of the colon, now another, and it may be further stated that the condition may be spastic or hypersecretive. The dominant symptom in the majority of cases is not acute pain, but a burning sensation. At times the pain is quite severe, occasionally crampy. There is generally tenderness over the ascending or descending colon. Backache is an invariable accompaniment. Constipation is the rule. The stools are small in the spastic type, large and covered with inspissated or glary mucus in the hypersecretive type. In this respect, mucous colitis of allergic origin does not differ from colitis from other causative agents. The pain or tenderness may be fixed over the cecal region, thereby resembling appendicitis or pyelitis; or a pendulous cecum may closely resemble right tuboovarian trouble. If the pain is permanently fixed at the hepatic flexure, cholecystitis may be suspected. When the transverse colon is affected, the symptoms may cause one to suspect gastric disease; and involvement of the splenic flexure may give the patient severe precordial pain, with a fixed idea that she is suffering from cardiac disease. Sigmoid involvement closely resembles the ovarian diseases, or may cause one to suspect diverticulitis, or pyelitis. Not infrequently an extension of the process to involve the rectum, causes tenesmus and exacerbation of any hemorrhoidal symptoms. The fact that the symptoms most frequently are not fixed, but pass from one colic area to another, almost at once leads one to suspect the correct cause. Palpation of the colon reveals general or local tenderness over the colonic area. The colon may be distended, or more frequently, present the hardness of a hawser. Constipation is the rule, with occasional bouts of bowel hyperactivity. There is always improvement after such a development. Upon awakening, there is a general abdominal soreness, and upon rising, backache and occasional articular rigidity.

A painstaking history, both personal and familial as to allergic susceptibilities, will greatly help in determining the proper cause. Alternating periods of recovery and recrudescence characterize the majority of cases. Patients are generally much more uncomfortable at the before or during the menstrual epoch.

Referred gastric symptoms are not uncommon. These are generally of the nature of nausea and eructations several hours after meals, or tremendous bloating.

Direct gastric symptoms are very varied, and may simulate organic gastric diseases so closely as to defy clinical differentiation. It is only by a process of exclusion, by tests of gastric function, which is not disturbed in allergic diseases, and by a suggestive personal and familial history of allergic manifestations, that the true nature of the dysfunction may be opined. In infancy, one of the commonest manifestations is pylorospasm, and regurgitation. In childhood, incipient hunger, followed after a small quantity of food, by an anorexia; in adult life,

symptoms simulating gastric ulcer without hematemesis or the acute local tenderness, torpitude and flushing of the face after meals, palpitation and profound muscular and mental lassitude.

Hepatic Allergy.—Probably the most interesting type of spastic allergy is that which affects the bile passages, simulating hepatic colic and probably pancreatic regurgitation. These cases are moderately common. They have come under observation in the last year. The symptoms are those of hepatic colic. The pain is right-sided, referred to the breast, shoulder and back; occasionally (in one case) the pain had the distribution also of involvement of the pancreas, in that the pain radiated also distinctly to the left of the mid-epigastric line. The history suggests gallstones so closely that all the patients were operated upon for this diagnosis, without finding stones at operation or in skiagraphs. The history of one of these cases will do more to clarify this syndrome than any other enumeration of findings. The patient, a physician's wife, mother of three children, had five distinct and severe attacks characteristic of hepatic colic. X-rays were negative. Tipp test negative. But owing to their characteristic onsets and the severity of the symptoms, non-opaque gallstones became the final diagnosis. Operation revealed a perfectly healthy gall bladder and bile passages. The gall bladder was removed. Patient made an uneventful recovery. Three months later she had a severe recurrence, and six months later another. She then came under the writers' care for a menstrual disturbance of allergic origin. She gave a familial history replete with allergic manifestations. Her husband, the doctor, is also allergic, all her children are allergic. She herself had a minus 18 basal rate, and was devoid of gastric free hydrochloric acid. She had most distressing attacks of migraine. After being under observation, but before the diagnosis was made, she had two severe colic attacks. The second lasted almost three hours. In the attack, three-fourths of a grain of morphine only aggravated the symptoms. Morphine, it is interesting to note, raises the intrabiliary pressure. She now learned that these attacks invariably followed the use of compound tablets of aspirin, phenacetin, caffeine and codeine, which she took for her migraine and facial neuralgia. Since this determination, she has been wholly free from biliary attacks. Since being placed upon XXX minims of hydrochloric acid and 4 gr. of thyroid (Burroughs Wellcome) t.i.d.p.c., she is no longer appreciably allergic, being free from migraine and eschewing aspirin. It may be interpolated that aspirin is a very common allergen in susceptible patients.

Two other cases gave a history somewhat analogous. A fourth came into the surgical wards of St. Mary's Hospital and under the care of the surgical resident, Dr. MacCormick, who has had an extensive training in allergy at the Children's Memorial Hospital. X-ray and other tests were negative. Amyl nitrate and later adrenalin gave immediate and complete relief. Later it was found that the allergen was a food product. Its deprivation prevented a recurrence. In all these cases the condition seems to point to a spasm of the sphincter

of Odie, and an elevation of intrabiliary pressure. Corroborative proof of this was found in the exacerbation of the condition by the use of morphine and its immediate relief by the antispasmodics, and by making the patient nonallergic, either by correcting the existing endocrine dysfunction, or by finding the causative allergen which disposes to allergic susceptibility. It was clearly pointed out in the previous paper, quoted above, that endocrine dysfunction often becomes the exciting factor in predisposed individuals, and the correction of the endocrine dyscrasia removes the susceptibility to allergens. It was also pointed out that the allergic state is familial or acquired, and is, in these cases, the constant subsoil which comes to the surface when the general health is lowered by disease or deranged function. Nothing in the human metabolism is left to hazard, each function being under the control of another function and it, in turn, under another. The final arbiters are the endocrines. Dysfunctions of these are the



Fig. 1.—Coagulated and liquid edema of the fimbriae. The empty spaces and dilated subfimbrial lymph channels were originally filled with liquid lymph. Coagulation has occurred only at the periphery.

necessary precursors of metabolic upsets. Under these dysfunctions of malnutrition of cell and body generally, familial, or acquired, allergic susceptibility may become a dominant factor in diseased states.

In the patient who had severe pain referred also to the left side, the inference was drawn that the intrabiliary pressure caused a back pressure along the duct of Wirsung into the head of the pancreas, thereby causing acute edematous pancreatitis, a condition so clearly described by Dr. Edward Archibald in "Acute Edema of the Pancreas" (*Ann. Surg.* November, 1929).

Allergy of the Peritoneum.—There are a few of these cases that are of minor degree. In a previous paper allergy of the pelvic cavity was fully described, especially when combined with pelvic inflammatory disease. However, allergy of the peritoneum may be general, without other signs of local disease, or the allergic extravasation may be local-

ized to any special part. Especially prone to this local manifestation are the Fallopian tubes at the fimbriated ends. (Fig. 1.) In the cases where the peritoneum, visceral and parietal, is involved, the edema is variable in quantity, in one case presenting a truly water-logged condition (Figs. 2, 3, and 4). In another case described by a colleague, the peritoneum was like a soaked sponge. Under these circumstances, the peritoneum, being indifferently securely attached to its underlying



Fig. 2.—Normal peritoneum.

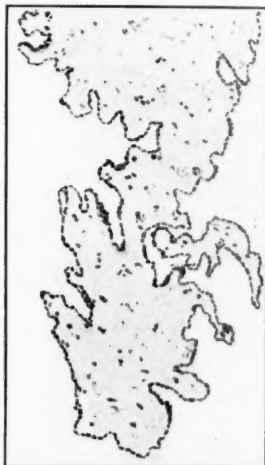


Fig. 3.—Slight peritoneal edema.



Fig. 4.—Allergic edema of the peritoneum, showing coagulum and liquid spaces.

structures, is thrown into numerous edematous convolutions which are covered by a single layer of flattened cells. Drawings of these demonstrate this condition very clearly. In other instances, the sections show the extravasated lymph in the widely dilated lymph spaces of the Fallopian fimbriae. In one case, a child of 7 years, very allergic, the peritoneum was as though it had been infiltrated everywhere by a syringe.

Cardiac Allergy.—This condition can be diagnosed only by the history of allergy, symptoms, and recovery under appropriate treatment. The cardiac symptoms may vary from precordial pain to acute pseudo-anginal attacks with a residual of pain that may last for twenty-four hours or more. Several of these cases have come under observation in women of allergic traditions, in whom appropriate treatment has immediately relieved the spasm, and removal of the offending agent, or a correction of the defective metabolism, has led to permanent relief. It is thought by general pathologists that many of the cases of cardiac death, without demonstrated coronary disease, and more especially in children, are probably allergic in character. In Goodall's paper on the toxicity of colitis, cardiac distress and fear of impending death are fully described.

How frequently one finds among physicians and others, signs of acute and chronic cardiac distress due to the allergic cardiac effect of a focus of infection, the removal of which gives almost immediate release from both fear and pain. Mention need hardly be made of the pulmonary complications of allergy: asthma, bronchitis, pulmonary and laryngeal edema, and lingual and oral swelling.

An obstetric patient was admitted to the private ward, in what proved to be false labor. For economic reasons, a therapeutic induction was attempted with castor oil and pituitrin, beginning with 2 minims and increasing 1 minim every half hour until a dose of 7 minims was reached. It proved ineffectual. She returned to the hospital ten days later in true labor. When about fully dilated, with membranes ruptured, labor pains ceased, and the resident later gave her 3 minims of pituitrin. Within one-fourth of an hour the patient was cyanotic, her lips were twice their natural size, the tongue was swollen twice its normal dimensions, the face was edematous, there was air hunger due to laryngeal edema, and both lungs were filled with moist, diffuse râles. The condition was suddenly critical for both mother and child. Oxygen and helium were used with good effect, and after the administration of 5 minims of adrenalin, the patient quickly recovered. Her temperature, meanwhile, shot up to 104° F., and the pulse was over 140, and the blood pressure rose rapidly from 110 to 150.

In another case the patient, a graduate of the Montreal Homoeopathic Hospital, who had known that she was allergic to certain drugs, was given a hypodermic of morphine on her second day post partum. Within an hour, her face was swollen almost beyond recognition. The conjunctivae were so edematous that they hung in wrinkles. The tongue was half as large again as normal. Dyspnea supervened, and her temperature rose to 105° F., with a severe chill. Adrenalin quickly controlled the discomfort, and in twenty-four hours the patient was back to a quasinormal state.

Muscular Allergy.—Allergic muscular dystrophies are very common. One has but to recall the muscular spasm of asthma, to realize what a profound and persistent effect this may produce. But one finds muscular spasm of an allergic nature under many and varied pathologic states. The writers wish to draw attention to the muscular spasms of pregnancy, which are an expression of a toxicity-producing allergic spasm. The percentage of women who suffer from these painful spasms of the legs, thighs, and feet, is very high. The spasm is acute for a time, frequently leaving a soreness which may last some hours, even days. These are so common as to be regarded as something to be expected and endured. They are an expression of toxicity, and

many spasms of a similar nature in other parts of the body, especially in the abdominal wall, intestines and uterus, are frequently complained of without ever a thought being given as to their true character. These are extremely common, and of unusual interest. They tend to recur in the same spot, when that area has once shown its susceptibility to its pregnancy change of environment. The muscles of the loins are particularly prone to this type of spasm, but any musculature may be involved. In two cases, the clinical interest is great, owing to the doubt which attended the cases until the proper diagnosis was established.

The first was a multipara, 38 years of age. Ten days before an anticipated delivery, she was seized with an excruciating pain in the right loin. Upon examination, there was no marked tenderness, slight rigidity, but the subjective symptom was intense. Morphine, $\frac{1}{4}$ gr., did not relieve at all, nor did a repeated dose effect any appreciable change. The pain gradually subsided, leaving a very marked soreness. Patient described it as a cramp. There had been no gastrointestinal disturbance, and a catheter specimen proved negative. The pain and soreness gradually wore off. A week later, I sectioned her and carefully examined all the organs of the right abdomen, without finding anything that offered an explanation. However, when coming out of the anesthetic, the patient again awoke to this fearful pain, which again was similarly localized, and would not respond to morphine. Suddenly its true character was defined, and the patient was given almost magical relief, by the administration of adrenalin.

In another somewhat similar case, the spasm of the oblique muscle could be distinctly felt. It was promptly relieved by adrenalin. Such abdominal spasms in the majority of pregnancies fortunately are of short duration, and do not require treatment. But it is well to be au fait as to their true character, and to the knowledge that they can be relieved, but not by morphine or other narcotics; antispasmodics would be a more logical procedure.

Cerebral Allergy.—Last, the effects of allergy upon the central and peripheral nervous system. In the previously quoted work on allergy, the authors described a case of allergic paresis during pregnancy, due to excessive extravasation of fluid from the choroid plexus. It is now well recognized that allergic edema of the brain is extremely common, rarely expressing itself in convulsions, but commonly in migraine, hemicrania, hemifacia, neuritis, papillary and conjunctival edema.

DIAGNOSIS

The diagnosis will rest upon the history. A meticulously careful inquiry into the personal and family history for some of the stigmas of allergy is one of the most important preliminary steps. The presence or absence of hay fever, asthma, bronchitis, eczema, prurigo, local edemas, acute poisoning by certain food producing vomiting bouts, neuralgias, and migraine, especially at the time of menstruation should be noted. These should be followed by a careful physical examination, including all the sense extension means to exclude organic disease. The basal metabolic rate should be established, and when normal, if the clinical picture of allergy is convincing, the thyroid therapeutic test will frequently prove that the metabolic estimation is wrong. The writers invariably add 10 to a minus reading and subtract 10 from a plus,

thereby getting, it is thought, a fairer record of actual states by allowing for the nervous excitation of a first test. Allergics are notably hypothyroids, and a large number of them are achlorhydries, so that before and after meals gastric free acidity test is essential, unless one applies the therapeutic test. Anemias are frequently profound and a distinct shift to the right, especially due to eosinophiles, is not uncommonly found, particularly during an attack. A blood sugar estimate must never be overlooked.

One of the worst cases of flaming vulvitis was encountered recently, in which the urine, on repeated examination by her physician, which had always been negative, showed blood sugar of only 98 m.g. before meals and after eating testmeal record of 119 m.g. Insomnia from the pruritus was almost dementing. She responded promptly to 5 unit doses of insulin, and was free from symptoms, but not of local discoloration, in five days.

TREATMENT

It will be found that a large percentage of allergies are facultative, conscious of discomfort only when the general health has sunk below the reserve of a gland, or of any system. In these it is but necessary to build them up so that they are again within their reserve, to bring about a clinical submergence of the allergic state. It cannot be too emphatically stated that these temporary allergic states, frequently accompanied by the most distressing symptoms, are due to a vitiation of function, brought about by a great diversity of activating causes, and it requires but the removal or correction of this cause, or causes, to submerge again the constant factor of hereditary allergic susceptibility. Nor can it be too strongly emphasized that no function of the body is left to hazard. Each and every function, no matter how insignificant, is under control. This control is generally vested in the endocrines, or in katalytic substances, the reduction or absence of which precipitates a vitiation and a consequent poisoning of the system, so that the lowered nutrition which follows, permits an emergence of the hereditary taint. In the vast majority of instances, it is but necessary to correct the dominant defect to re-cover the hereditary subsoil. Thyroid is the dominant endocrine dysfunction in these cases, and fortunately it is almost always a deficiency disease, so that supplemental administration of the extract becomes a simple procedure. Whether this is merely an accidental association, it is impossible to state with any degree of assurance, but the association of the two conditions is so common, beyond any possibility of explanation by the law of chance, that there would seem to be a decided interdependence, as cause and effect, or due to a common cause. However, the establishment of these associated defects gives one a ready means of treatment, by thyroid and hydrochloric acid. The allergic response is usually prompt and complete.

Glycemia should be excluded or, if present, treated appropriately. Anemias should be overcome. Parasitic intestinal diseases should be studied. Everything should be investigated to find a vitiating cause which did not exist when the patient was formerly nonallergic.

The chronic cases, frequently allergic to many things, are the most deserving of our keenest study. They are highly susceptible cases, in which the hereditary influence is usually pronounced, and in which the hereditary subsoil is constantly, slightly, or much exposed.

They have a multiplicity of symptoms, affecting now one system, now another, dyspnea, tachycardia, arrhythmia, migraine, neuritides, gastric disturbances, colitis, spastic dysmenorrhea, menorrhagia and metrorrhagia, articular pains, etc. They constitute the great majority of our so-called neurasthenics. The contributing cause for aggravation may be economic, moral, mental, or emotional. They are not the self-pitying type, but, being conscious of their unwonted irritability, generally state that they are sorry for their husband or their children.

Frequently a change of scene, and a freedom from household cares, bring about almost magical changes. Other cases will frequently tax one's ingenuity, as well as one's patience, to the utmost limit. When improvement is brought about, it is usually temporary. Relapses are frequent and discouraging.

REFERENCES

- (1) Goodall, James R.: J. Obst. & Gynaec. Brit. Emp. 43: 925, 1936. (2) *Idem*: AM. J. OBST. & GYNEC. 33: 194, 1937.

WEIGHT CHANGES AND TOXEMIA OF LATE PREGNANCY*

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IN 1916 Zangemeister suggested observations on the weight changes of pregnant women for the detection, through large increases, of latent, occult, or preclinical edema, which he believed to be a sign of incipient toxemia of pregnancy. Since that time there have appeared a number of articles which have largely supported Zangemeister's recommendation. Some have even gone so far as to suggest regular weighing as not only highly valuable in predicting toxemia but also as a reliable means for the actual diagnosis of the established disease. A critical study of these articles shows that, with few exceptions, there is little more than authority of other authors or clinical impression to justify the views expressed. Where statistical evidence has been presented, it is frequently unconvincing or questionable because of insufficient numbers, lack of comparison with normal cases, or other reasons.

A previous study by us⁵ presented, among other data, evidence against too great enthusiasm regarding the value of weighing for the early diagnosis of toxemia. Although excessive weight gains did precede the signs (hypertension and albuminuria) of frank toxemia in about

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40 per cent, similar gains occurred at some time in approximately the same proportion of our normal patients. In the remainder of the patients with toxemia, excessive gains were noted for the first time coincident with or well after the onset of the disease, or not at all. These findings were so contrary to our expectations (based on the literature and our own clinical impressions) that, striking as were the results, we considered the possibility of error due to the small number (39) of toxemia cases studied. Consequently, we have assembled 61 additional cases to make a series of 100. Fifty of these occurred in our practices, while the remainder were obtained from the records of Drs. George Kamperman, Ward Seeley, and Harold Henderson whose kind permission and cooperation we wish to acknowledge.

In this series of 100 we included only patients with unquestionable toxemia as shown by systolic blood pressure of at least 140 mm. of mercury plus definite albuminuria. We eliminated all patients with multiple pregnancy and those with any disease or condition which could be expected to affect the weight. Furthermore, these were private patients of the white race, native born for the most part, and with no economic necessity for limitation of diet. Only patients who were weighed regularly up to term or within a few days of premature delivery were included. Also, in order to insure as high a degree of accuracy as possible, a clear and definite history of the last menstrual period was considered essential. Our calculations were made from weights taken at the twenty-fourth, twenty-eighth, thirty-second, thirty-fourth, thirty-sixth, thirty-eighth, and (in 47 cases) fortieth weeks.

The selection of case records conforming to the above criteria permitted a fair comparison with the series of normal patients in our former report. The fact that Cummings from the same region and with a similar type of patients obtained averages almost identical with the normals in our previous study supported our confidence in the reliability of those figures. With this exception, we have avoided weight for weight comparisons with series of other authors, though general trends and conclusions have been noted. We considered this to be a precaution in the interests of accuracy since the types of patients in various series differ so greatly. Certainly, for a number of reasons, private patients cannot be fairly contrasted with clinic patients. Furthermore, it is quite possible that factors such as race, nationality, and even locality are of importance in affecting weight gain.

Our former study, though showing numerous unexplained and often extreme deviations from the averages, indicated that age had definite influence on weight changes. Parity was also of some importance, but body build (or height-weight ratio) much less so. Consequently, as information regarding age and parity was available for the 100 toxemia patients, allowance for these factors was made in certain of the calculations by comparing each abnormal case to the averages for the corresponding age and parity group of normals. Actually, however, this precaution had no great effect on the final results.

Of the 100 toxemia patients, 69 were primiparas. In 24 there had previously been one, and in 7, two or more term or premature deliveries. Determination of the types of toxemia offered the usual difficulties, but from the excellent records, not only for the present but also in many for past or subsequent pregnancies, it appeared that 55 had so-called "low reserve kidney," 20 chronic nephritis, 17 pre-eclamptic toxemia (pre-eclampsia), and 8 eclampsia.

The average gain in weight for the 100 toxemia patients during the last four lunar months of pregnancy was 17 pounds as compared to 15.7 pounds for the normals. In Table I the average gains during each observation period are given for the toxemia patients and for the normal patients from the previous report. Naturally, toward the latter part of pregnancy the averages were obtained from a diminishing number due to premature deliveries, though even at term there were 47 weights on toxemia patients.

TABLE I. AVERAGE WEIGHT GAIN IN POUNDS

WEEK	24-28	28-32	32-34	34-36	36-38	38-40	TOTAL
100 Toxemia	4.3	4.8	3.0	2.3	1.4	1.2	17.0
624 Normal	4.4	3.9	2.0	2.1	2.0	1.3	15.7

Since the foregoing figures run somewhat contrary to the usual opinion when they indicate only moderate increase in weight gain for toxemia, we considered the possibility that single or even several excessive gains occurring at different times among the patients might be concealed or masked, so to speak, in the averages. Consequently, each patient's record was examined for excessive weight gain at the above designated observation periods. Inasmuch as our previous study (confirmed by McIlroy and Rodway, and others) demonstrated many deviations from the averages even in normal patients, we selected twice the average (or more) as a practical figure to indicate excessive weight gain. Comparison was made with Table V of our previous paper, thus taking into consideration the factors of age and parity. This showed that 61 of the 100 toxemia patients had excessive weight gains to this extent at one or more times after the beginning of the seventh lunar month. The remainder of the cases, or the substantial number of 39, had no excessive gain at any time. Indeed, it is interesting to note in view of Zangemeister's observations on "hydrops gravidarum" that seven of these patients did not at any single observation period show a gain above the averages. Moreover, the average increase in weight during the last four lunar months for the group of 39 without excessive gain was only 11.6 pounds as opposed to the normal average of 15.7 pounds.

In order to investigate the possible variation in severity of toxemia in relation to the presence or absence of excessive gain, the disease was classified as mild when the highest systolic blood pressure was below 150 mm. of mercury; moderate with blood pressure of 150 or above but below 170; and severe if 170 or above. True eclampsias were classified as "severe" regardless of height of blood pressure. The percentage incidences of these grades of severity among the 61 with excessive gain were: mild, 19.7; moderate, 49.2; and severe, 31.1 (including 6 eclamp-

sias). For the 39 without excessive gains the percentages were not greatly different, being respectively 20.5, 41.0, and 38.5 (2 eclampsias). (See Table II.)

TABLE II. SHOWING THE PERCENTAGE INCIDENCE OF MILD, MODERATE, AND SEVERE TOXEMIA WITH AND WITHOUT EXCESSIVE WEIGHT GAINS DURING THE LAST FOUR MONTHS OF PREGNANCY

	MILD TOXEMIA	MODERATE TOXEMIA	SEVERE TOXEMIA
With excessive gains (61 cases)	19.7	49.2	31.1
Without excessive gains (39 cases)	20.5	41.0	38.5

The relationship of the type of toxemia to excessive weight gains was inconclusive due to the small numbers of cases, though perhaps of some significance. The 55 "low reserve kidney" cases showed about the same ratio as the whole series, namely, 33 (60 per cent) with excessive gain at one or more observations, and 22 without. Nephritis complicating pregnancy was evenly divided, 10 with and 10 without. The 17 with pre-eclamptic toxemia (pre-eclampsia) showed 12 with and 5 without excessive gain. Six of the 8 eclampsias were associated with excessive increase.

As stated in the opening paragraph, regular weighing as a part of prenatal care has been advised repeatedly as an efficient means of predicting and thus forestalling the onset of toxemia, the idea being that definite signs of the disease are preceded in a large proportion of the cases by excessive weight gains due to occult edema. Most worthy of consideration in this regard is the recent study of Evans who not only agreed with this advice but even suggested the procedure as an excellent means of detecting fully developed toxemia, apparently considering it more useful than blood pressure observations and urinalysis. He stated that 82 per cent of toxemias could be discovered by weighing alone. It may not be amiss to point out that Evans' conclusions were based on the records of only 211 patients (apparently a series of consecutive cases) of whom the surprising number of 52 were classified as toxemia. Fifteen of these showed no albuminuria and therefore did not meet the usual criteria for toxemia of pregnancy. However, even if these patently doubtful cases are eliminated, there still remain 37, an unusual toxemia incidence of 17.5 per cent, or 1 in 6 pregnancies. The incidence at Harper Hospital (private and clinic) during the last four years has been 4.4 per cent, including some patients who, but for the toxemia, would have been delivered elsewhere. McIlroy and Rodway go so far as to state that they have prevented many cases of toxemia by alertness in respect to large gains and the institution of prophylactic treatment. Though not denying this as a possibility, we believe their statement would be more credible if they could show an untreated control series for comparison, especially since another section of their paper confirms our previous study in showing that there are many patients who have excessive weight gains and yet go to term without toxemia.

Examination of our 100 toxemia cases showed that among the 61 with excessive gain there were 37 in which this *preceded* definite signs

of the disease. It *coincided* with hypertension, albuminuria, or both 15 times, and it *followed* the appearance of these signs in 9. To obtain a complete picture, we must consider the whole group, including the 39 without excessive gains at any time. In Table III it is seen that besides the 37 in which excessive weight increase appeared first, the earliest evidence of toxemia was: hypertension, 22; hypertension and albuminuria, 18; excessive weight gain with hypertension and sometimes also albuminuria, 15; and albuminuria alone, 8. (As there were 100 patients in the group, percentages are of course the same as the case incidences.)

TABLE III. EARLIEST SIGNS OF TOXEMIA IN 100 CASES

SIGNS:	EXCESSIVE WEIGHT GAIN	HYPERTENSION	HYPERTENSION AND ALBUMINURIA	EXCESSIVE WEIGHT GAIN HYPERTENSION ALBUMINURIA	ALBUMINURIA
Number and percentage	37	22	18	15	8

Calculations from Table III apparently suggest that as the earliest indication of toxemia, excessive weight gain (52 cases), either alone or combined with other signs, approximates in value the appearance of hypertension (55 cases), albuminuria being of much less importance. Furthermore, since excessive weight increase preceded other signs in 37 per cent of the toxemias, it might seem of real value in discovering the disease in its incipency. A practical difficulty in application, however, is found in the fact, frequently ignored, that a large proportion of normal patients also have these large gains. In our previous report 280 of 624 normals (about 45 per cent) showed this excessive gain one or more times during the last four lunar months and were delivered at term without any evidence of toxemia. Consequently, our figures indicate that acceptance of excessive gain as reliable evidence of incipient toxemia necessitates subjecting approximately one-half of all pregnant women to treatment. A comment⁷ on our previous study that, "It is easy to tell if the gain in weight is due to water or fat," is not in accord with our experience, or apparently that of others, since the water retention we are here largely concerned with is hidden or occult and not demonstrable as edema. Incidentally, it may be mentioned that, in addition to large weight gains, we also see various degrees of edema in a fair number of otherwise normal patients, sometimes without much weight increase. Furthermore, it is most common and most marked in warm weather when toxemia is said to occur least often. Finally, a considerable number of patients with definite, and even severe, toxemia show no edema, either demonstrable or occult.

Those who, in spite of the foregoing data, may be convinced of the advisability of prophylactic treatment in patients with excessive weight

gains will find a confusing and often contradictory list of recommended procedures, such as: general restriction of caloric intake; full feeding in malnourished patients; specific limitation of proteins, carbohydrates, fats, or salt; a diet of milk only; endocrine gland products; restriction of water intake; forcing of large quantities of fluids; strict bed rest; and increased bodily exercise, to mention a few. Harding and Van Wyck believed their regime consisting of a salt-poor, low caloric diet, restricted fluid intake, and bed rest explained their low toxemia rate. We have found this treatment of value in combating water retention and edema but consider its efficacy in preventing actual toxemia as not yet clearly proved.

Some authors, while ascribing great importance to large weight gains, have further stated that lesser gains also have some significance. Among our 100 toxemia patients there were, in addition to the 61 with excessive gains, another 20 with weight increases at one or more periods exceeding the averages by 50 per cent or more. A glance at Table II of our previous report shows that such gains were also frequent with normals. Furthermore, an examination of 100 unselected normal patients showed that, besides the 40 with excessive gains, there was among the remaining 60 a group of 28 who had gains of at least 50 per cent above the averages one or more times during the last four months. The proportion, then, for toxemia (20 out of 39) was only slightly greater than that for the normals (28 out of 60).

Several observers have stressed the *sudden* large weight gain as particularly indicative of impending toxemia. A study of our 61 toxemia patients with excessive gains showed that there were 17 in which the gains could be considered sudden and unexpected as they were preceded for one or more observation periods by average or less than average increases. A second group of 29 had excessive increases which were less abrupt, since the previous gains were more than average though less than 50 per cent plus. The remaining 15 had excessive gains following large increases of 50 per cent or more above the average and therefore were in no way sudden or unexpected. As a comparison, 100 normal patients (unselected except for parity to correspond with the toxemias) showed 40 with excessive gains, of which the numbers occurring in the above three groups in order were 8, 15, and 17. The percentage incidences for the toxemia and normal patients with excessive gain were: First group (with sudden gain), toxemia 27.9—normal 20.0; Second group (less sudden), toxemia 47.5—normal 37.5; Third

TABLE IV. A COMPARISON BETWEEN NORMAL AND TOXEMIA PATIENTS IN REGARD TO THE SUDDENNESS OF EXCESSIVE WEIGHT GAINS—AS EVIDENCED BY THE EXTENT OF PREVIOUS WEIGHT INCREASES

	PATIENTS WITH EXCESSIVE GAINS	
	NORMAL (40)	TOXEMIA (61)
Increase average or less than average before onset of excessive gain	20.0%	27.9%
Increase more than average but less than 50 per cent plus before excessive gain	37.5%	47.5%
Gains of 50 per cent or more above average before excessive gain	42.5%	24.6%

group (with preceding gains well above the average), toxemia 24.6—normal 42.5. (See Table IV.) It is apparent, then, that a sudden large increase in body weight is somewhat more common among toxemia patients than among normals, though it is far from the rule.

In presenting the foregoing observations, we do not wish to be understood as condemning routine prenatal weighing as useless. Indeed, it is of value other than in its possible relationship to toxemia. However, so far as toxemia is concerned, we do feel that the significance of excessive weight gain has apparently been misunderstood or greatly overrated. Our data show it to be far from reliable as a sign of impending toxemia. And, though we will agree that routine weighing may be considered as a possible adjunct in detecting the actual disease, it can by no means replace established procedures such as routine blood pressure determinations and urinalyses.

SUMMARY

A series of 100 private patients with definite toxemia of late pregnancy had an average gain in weight of 17 pounds during the last four lunar months of pregnancy, as compared to 15.7 pounds for normals. Sixty-one of these 100 toxemia patients gained at least twice the normal averages at one or more observation periods during this time, while 39 at no time showed such excessive gains. The presence or absence of excessive weight increases bore little or no relationship to the severity or to the type of the toxemia. In 37 patients, excessive weight gain preceded definite signs of toxemia, but in the remaining 63 it appeared along with or after these signs, or not at all. Moreover, it was also present in about 45 per cent of the normals. Sudden or abrupt weight increase was somewhat more frequent with toxemia than among normal patients but was far from the rule. The occurrence of excessive weight gains in pregnancy would appear to be of doubtful significance in predicting impending toxemia and of secondary value, at most, in the diagnosis of the actual disease.

REFERENCES

- (1) *Cummings, H. H.*: AM. J. OBST. & GYNEC. 27: 808, 1934.
- (2) *Evans, M. D. A.*: Brit. Med. J. 1: 157, 1937.
- (3) *Harding, V. J., and Van Wyck, H. B.*: Canad. M. A. J. 30: 14, 1934.
- (4) *McIlroy, A. L., and Rodway, H. E.*: J. Obst. & Gynaec. Brit. Emp. 44: 221, 1937.
- (5) *Siddall, R. S., and Mack, H. C.*: AM. J. OBST. & GYNEC. 26: 244, 1933.
- (6) *Zangemeister, W.*: Ztschr. f. Geburtsh. u. Gynäk. 78: 325, 1916.
- (7) Year Book of Obstetrics and Gynecology, Chicago, 1933, The Year Book Publishers, p. 18.

UNSUSPECTED TUBERCULOSIS IN PREGNANT WOMEN AS REVEALED BY ROUTINE ROENTGENOLOGIC EXAMINATIONS*

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WHEN pregnancy occurs in a woman who has tuberculosis, a serious problem confronts the physician. It is not our purpose to review the extensive literature on this subject. However, the opinion is generally held that pregnancy creates a grave additional hazard for the tuberculous woman, and it may aggravate the disease and even menace her life. Furthermore, the newborn baby of a mother with undiagnosed tuberculosis is very likely to contract the disease from its mother. Conservative estimates have placed the incidence of active tuberculosis in the "healthy" population at 1.5 per cent.¹ It is only reasonable, then, that our standards for efficient prenatal care should include an effective method for detecting the presence of tuberculosis. It is our purpose to present data which indicate that sufficient unsuspected tuberculosis can be found by routine chest fluoroscopy to justify its use in all prenatal patients.

There has been a growing conviction of the inadequacy of the physical examination as a means of detecting the presence of pulmonary tuberculosis and the importance of roentgenologic diagnosis has been ever increasing. Responsible physicians will no longer rule out the presence of pulmonary tuberculosis on the basis of a physical examination alone, for they realize that even the most skilled examination often fails to reveal the presence of significant pathology.

This fact has been demonstrated by various workers in the field of tuberculosis. Kayser-Petersen's recent extensive review² indicates that from 10 to 60 per cent of all cases of tuberculosis which were found on x-ray examination had been missed on physical examination. Five years ago, Bloch estimated, on the basis of the experience of the chest division of the University of Chicago Clinics, that about one-third of all cases of clinically important lung disease are missed on physical examination.³ Now he believes that one-third is too conservative an estimate.¹ Sampson and Brown⁴ in their careful study of 1,004 patients at Trudeau Sanatorium found no physical signs of disease in 39.6 per cent, and physical signs indicating less disease than the roentgenogram in an additional 36 per cent.

The absence or scarcity of symptoms is increasingly acknowledged as another cause of failure to make the diagnosis of tuberculosis in many cases. Tuberculosis which has not advanced into the stage of tissue

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Part of this paper was taken from a more comprehensive report of group roentgenologic examinations made at the University of Chicago Clinics. A complete report of the data obtained in this survey entitled "Roentgenological Group Examinations for Pulmonary Tuberculosis" by Bloch, Francis, Eisele and Mason, was presented at the Fifth International Congress of Radiology, in Chicago, September, 1937, and was published in "The American Review of Tuberculosis" 37: 174, 1938.

necrosis rarely causes noticeable symptoms. The public is only inadequately served by so-called "early diagnoses" campaigns urging individuals with certain symptoms to submit to an examination. The most such efforts can accomplish is to uncover a limited number of well-advanced cases. An amazing number of people with extensive and occasionally spectacular disease do not have enough symptoms to arouse the suspicions of the patient himself, his family, or even his physician. It is significant that more than 80 per cent of all cases of tuberculosis reported to health departments are already in an advanced stage.⁵

The logical conclusion is that in order to find tuberculosis at an early stage—to find it reliably at any stage—it is necessary to make the roentgenologic examination routine even for "healthy" persons.

In 1932 Bloch and his associates in the chest division of the University of Chicago Clinics began a series of roentgenologic group examinations on students and employees. In 1934 they widened the scope of this work to include the patients attending the prenatal clinic of the Chicago Lying-in Hospital. These patients were invited to report to the Chest Clinic for a fluoroscopic examination free of charge. Of the 6,298 patients attending the prenatal clinic from Feb. 14, 1934, to April 1, 1937, 4,040, or 64 per cent, reported for this examination (Table I). These patients were unselected except for the exclusion of known or suspected cases of tuberculosis. The entire group were of the white race. All patients showing definite or suspected lesions by fluoroscopy were referred for stereoscopic roentgenograms. Seventeen patients in whom tuberculosis was suspected on fluoroscopy did not report for roentgenograms. Forty-three, or 1.06 per cent, of fluoroscoped group were shown to have tuberculous changes of clinical importance. Of these 28, or 0.7 per cent, had active tuberculosis. We would like to emphasize that these cases of tuberculosis were unsuspected. It is not probable that they would have been diagnosed if routine fluoroscopic examinations had not been carried out.

We believe that in order to obtain fully satisfying results, these examinations will have to be made obligatory.* Four of the 17 patients who had fluoroscopic findings but no roentgenograms canceled their clinic registration when asked to have chest films. It seems to us that the percentage of active tuberculosis might have been higher if all the clinic patients had been fluoroscoped, for it is probable that some of these women refused roentgenograms because of the fear of tuberculosis, and some may even have been attempting to conceal past disease.

In addition to tuberculosis, several nontuberculous pulmonary and extrapulmonary conditions were found. Cardiac enlargement or pathologic cardiac contour was described in 205 cases and suspected in an additional 170 cases. In these, organic heart disease was diagnosed clinically in 181, or 4.5 per cent, of the fluoroscoped cases. We attribute this discrepancy to the fact that the cardiac displacement in late pregnancy may simulate cardiac enlargement on fluoroscopy. There were also three cases of bronchiectasis, and one case each of substernal thyroid, calcified thyroid, calcified pleura, tumor of the pleura, and spontaneous pneumothorax.

The reliability of chest fluoroscopy as a case finding method in tuberculosis has been questioned by some on the basis that it is too subjective

*At the present time we are fluoroscoping nearly 100 per cent of the prenatal patients by making this procedure a part of their general examination on their first clinic visit.

and therefore is open to error. However, it has been noted that the accuracy of the method increases directly with the increased experience of the examiner.¹ The superiority of chest roentgenograms over fluoroscopy cannot be questioned, but the expense of films has made it impractical for many group examinations. Most authors agree that excellent results can be obtained with fluoroscopy if roentgenograms are made on all persons with definite or suspicious findings fluoroscopically. We do not believe that many tuberculous lesions of clinical importance are overlooked by an experienced examiner who is trained in fluoroscopic technique and in lung pathology. However, it is true that in inexperienced hands considerable pathology may be missed. Certainly all

TABLE I. ROUTINE FLUOROSCOPIES ON UNSELECTED CASES (EXCEPT FOR THE EXCLUSION OF KNOWN TUBERCULOSIS), BETWEEN FEBRUARY 14, 1934, AND APRIL 1, 1937

			NUMBER		PER CENT	
Total clinic patients			6,298		100.0	
Fluoroscoped patients			4,040		64.0	
Not fluoroscoped:						
No known tuberculosis			2,209		35.2	
Known tuberculosis			49		0.8	

I. TUBERCULOSIS			II. CARDIAC PATHOLOGY		
	NO.	PER CENT OF FLUOROSCOPED CASES		NO.	PER CENT OF FLUOROSCOPED CASES
1. Clinically important tuberculosis, proved by subsequent roentgenograms:			1. Fluoroscopic findings:		
a. Active	28	0.69	a. Hearts considered to be enlarged and/or of pathologic contour	205	5.1
b. Inactive	15	0.37	b. Hearts questionably enlarged and/or of pathologic contour	170	4.2
Total	43	1.06	Total	375	9.3
2. Suspicious findings but patients failed to get roentgenograms (4 patients canceled their clinic registration when asked to have chest films)	17		2. Final diagnosis in above cases:		
Summary:			a. Organic heart disease	158	3.9
Tuberculosis found on fluoroscopy	43		b. Probably organic heart disease	23	0.6
Known tuberculosis	49		Total	181	4.5
Total tuberculosis	92		c. No organic heart disease (apparent enlargement due to cardiac displacement in late pregnancy)	119	
If incidence of 0.69% was maintained there were 15 additional cases of active tuberculosis undiscovered among the unfluoroscoped patients			d. Inadequate observation for definite diagnosis	75	
			MISCELLANEOUS		
			NO.		
			1. Bronchiectasis		
			2. Substernal thyroid		
			3. Calcified thyroid		
			4. Calcified pleura		
			5. Tumor of the pleura		
			6. Spontaneous pneumothorax		

advanced tuberculosis can be diagnosed quite easily this way. It should be emphasized that the fluoroscopic examination is used only as a screen in case finding surveys, but never to rule out the possibility of lung disease where there are symptoms. Nor is it reliable for making a definitive diagnosis, or as a means of following the course of a tuberculous lesion. For these purposes, roentgenograms are essential.

Tuberculin tests as a screening method have been used instead of a roentgenological method chiefly in examining school children. Apparently they can be used successfully in children. It is not the purpose of this paper to compare the reliability of the tuberculin test and fluoroscopy as screening methods. However, we concluded that the fluoroscopic method would be more efficient in most adult groups. The first difficulty in applying the tuberculin test to adult groups is the necessity for a return visit at a specified time for the reading of the test. A lack of adequate patient cooperation on this point would probably lead to failure in many instances. An additional and more important objection is the fact that a large number of clinically nontuberculous adults react to tuberculin. In urban populations, a majority of adults are positive reactors. If a tuberculin survey is to be of practical value, it would be necessary that all positive reactors have a roentgenologic follow-up at considerable expense of money and time. At the same time a small percentage of clinically tuberculous people do not react, or react only very weakly, to tuberculin. We believe that present methods of tuberculin testing do not present us with as accurate a picture of the true status of adult clinical tuberculosis as the more direct roentgenologic method.

A study of the reported incidence of tuberculosis in comparable groups of obstetric patients (Table II) further substantiates the opinion that when physical examination and history taking alone are relied upon, even when carried out by careful clinicians, many cases of tuberculosis remain undiagnosed. Allen and Bauer⁶ reported the incidence of medical complications in 9,696 consecutive pregnancies from Presbyterian Hospital and Rush Medical College out-patient department (Chicago). They reported seven cases of tuberculosis, or an incidence of 0.07 per cent. Tamis and Clahr⁷ report that in 1,009 obstetric patients, seen during 1934 in the prenatal clinic of the Morrisania City Hospital (New York), no cases of tuberculosis were found. All were charity patients. Royston, Jensen, and Hauptman² report 51 cases of tuberculosis in 13,570 obstetric patients at the St. Louis Maternity Hospital and out-patient department, an incidence of 0.37 per cent. The authors point out that this is not a true incidence because some of the patients were referred from elsewhere because of the tuberculosis. It may be noted also that 19, or 37 per cent, of the tuberculous patients were negroes. At the Chicago Maternity Center⁸ 17,739 women were registered for confinement care in their own homes from July 1, 1932, to June 30, 1937. Approximately one-third of these patients were negroes. Ten patients were found to have tuberculosis (including two cases of tuberculous meningitis and one case of miliary tuberculosis). In ad-

dition, there were 8 cases of suspected tuberculosis which could not be followed adequately for final diagnosis. It is of interest that of the 21 maternal deaths occurring in this series, 5, or 24 per cent, were due to

TABLE II. THE INCIDENCE OF TUBERCULOSIS REPORTED IN OBSTETRIC GROUPS IN WHICH ROUTINE ROENTGENOLOGIC EXAMINATIONS WERE NOT MADE

AUTHORS	INSTITUTION	PATIENTS IN SERIES	CASES OF TUBER- CULOSIS	IN- CIDENCE PER CENT	COMMENT
Allen and Bauer	Rush Medical Col- lege O.P.D. and Presbyterian Hospital, Chica- go	9,696	7	0.07	
Tamis and Clahr	Morrisania City Hospital, New York	1,009	0	0.0	All charity pa- tients; negroes included
Royston, Jen- sen, and Hauptman	St. Louis Mater- nity Hospital and O.P.D.	13,570	51	0.37	Some referred from elsewhere because of tu- berculosis; 37 per cent of pa- tients with tu- berculosis were negroes
Tucker	Chicago Maternity Center	17,739	18	0.10	Ten cases proved; 8 cases suspect- ed. All patients registered for home delivery. About one-third of group were negroes
Total		42,014	76	0.18	

tuberculosis. It would seem that in all of these groups the economic and social status was equal to, or lower than, that of our group. Many negroes were included whereas our group was from the white race exclusively. In the combined groups, totaling 42,014 patients, there were 76 cases of tuberculosis (including suspected cases). If routine roentgenologic examinations had been made, one could reasonably expect six times as many cases.

Today one does not question the advisability of the use of routine Wassermann and Kahn tests to discover syphilis in pregnant women. The number of cases of unsuspected syphilis so discovered has more than justified making this a routine procedure. However, an equal justification for routine chest fluoroscopies has not hitherto been recognized. Therefore, we have compared the incidence of unsuspected syphilis with the incidence of unsuspected tuberculosis discovered by the respective routine examinations in our clinic. During the same period that our fluoroscopic survey was made, there were 139 patients with some degree of positiveness in either the Wassermann or Kahn, or both. After further serologic and clinical investigation, 45 of these were considered to be nonsyphilitic. Of the 94 remaining cases, 39 had previously received antisyphilitic treatment. Thus, there were 55 cases of unsuspected and

undiagnosed syphilis discovered by routine Wassermann and Kahn tests. This gives an incidence of 0.87 per cent for the 6,298 patients attending the clinic during this period. This figure is comparable to the incidence of 1.06 per cent of the unsuspected tuberculosis in our fluoroscopic series. It is a reasonable conclusion, then, that routine roentgenologic examinations of the chest rank with routine Wassermann tests as a medical necessity in pregnant women. One may argue that the problems of syphilis and tuberculosis in pregnancy are not the same, that syphilis is of greater importance because of the danger of transmission of the disease to the fetus. However, though prenatal infection of the fetus with tuberculosis has never been conclusively proved, and if it does occur, it is so rare as to be of no clinical importance, there is grave danger of the newborn infant contracting the infection from its mother.

In recent years, the much publicized decline of the mortality rate from tuberculosis has led to the belief that the disease is getting well under control. Although tuberculosis has moved from first to seventh place as a cause of death in the general population, for the age groups involving obstetric patients tuberculosis still ranks first as a cause of death.

SUMMARY AND CONCLUSIONS

1. The inadequacy of symptoms and physical examination as means of discovering pulmonary tuberculosis has been discussed.

2. Routine chest fluoroscopy, followed by roentgenograms in all cases with definite or suspected lung pathology, is a satisfactory method of finding tuberculosis when carried out by an experienced examiner trained in fluoroscopic technique and lung pathology.

3. Application of this method to 4,040 pregnant women, unselected except for the exclusion of known tuberculosis, disclosed 43 cases of unsuspected tuberculosis or an incidence of 1.06 per cent. Twenty-eight cases, or 0.7 per cent, were shown to be active during the pregnancy.

4. The incidence of 1.06 per cent for unsuspected tuberculosis is approximately the same as the incidence of 0.87 per cent for unsuspected syphilis discovered by routine Wassermann and Kahn tests carried out in the same clinic over the same period of time.

5. Routine chest roentgenologic examinations should rank with routine Wassermann tests as a medical necessity in pregnant women.

6. Tuberculosis in pregnant women is still an important problem, for tuberculosis remains as the leading cause of death in this age group.

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REFERENCES

- (1) Bloch, R. G., Francis, B. F., Eisele, C. W., and Mason, E. W.: *Am. Rev. Tuberc.* 37: 174, 1938.
- (2) Kayser-Petersen, J. E.: *Ergebnisse der gesamten Tuberkuloseforschung.* 8: 71, 1937 (Georg Thieme, Leipzig).
- (3) Bloch, R. G.: *München. Med. Wehnschr.* 2: 1900, 1932.
- (4) Sampson, H. L., and Brown, L.: *Radiology* 22: 1, 1934.
- (5) Vaughan, H. T., and Douglas, B. H.: *J. A. M. A.* 109: 771, 1937.
- (6) Allen, E., and Bauer, C. P.: *AM. J. OBST. & GYNEC.* 31: 885, 1936.
- (7) Tamis, A., and Clahr, J.: *J. A. M. A.* 109: 195, 1937.
- (8) Royston, G. D., Jensen, J., and Hauptman, H.: *AM. J. OBST. & GYNEC.* 34: 284, 1937.
- (9) Tucker, Beatrice E.: Personal communication.

AN EVALUATION OF THE SEDIMENTATION TEST IN THE
DIFFERENTIAL DIAGNOSIS OF ACUTE PELVIC
INFLAMMATORY DISEASE AND ACUTE
APPENDICITIS*

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THE study presented was undertaken for the purpose of evaluating the sedimentation test as a diagnostic aid in differentiating between acute pelvic inflammatory disease and acute appendicitis.

The conclusions are based upon a study of thirty patients with pelvic inflammatory disease and one hundred patients with acute appendicitis, admitted to the Receiving, Gynecological, and General Surgical Wards of the Jefferson Medical College Hospital from September, 1934 until November, 1937.

The value of the sedimentation test has been definitely established by numerous observers, and this is especially true in gynecology. The theories as to why the blood cells settle more rapidly in certain pathologic conditions, and less rapidly in others have been thoroughly discussed by various investigators, but there is apparent disagreement as to the actual cause. Nicholson¹ states in "Laboratory Medicine" that there is no adequate explanation of the phenomenon. A discussion of this phase of the subject is without the scope of this presentation; consequently this aspect of the problem will not be discussed.

We have observed over a long period of years that patients suffering with well-developed pelvic inflammatory disease always have a rapid sedimentation rate. This test, while possibly superfluous in making a diagnosis of advanced pelvic inflammatory disease, is valuable for other well-known reasons. Hence it occurred to us that if the test were performed at the onset of suspected acute appendicitis or acute pelvic inflammatory disease, before the diagnosis had been definitely established, it might prove to be of decided value. It is probable in most instances that the physician is called to see the patient with lower abdominal pain within the first twenty-four or forty-eight hours. This is the strategic time, when diagnostic acumen is often taxed to the utmost, for the patient may have a surgical abdomen, which if not cared for promptly may result in disaster. On the other hand, surgical interference may have harmful consequences, especially in the young woman of childbearing age. The (two) conditions which most frequently confuse the general surgeon and the gynecologist in establishing a differential diagnosis are acute appendicitis and pelvic inflammatory disease, in the early stage when the pain is still localized in the right lower quadrant.

*Read at a meeting of the Obstetrical Society of Philadelphia, January 6, 1938.

When our investigation was begun in 1934 there had been no studies recorded on this particular phase of the sedimentation test except those in an article published by Grodinsky.²

TABLE I. ACUTE PELVIC INFLAMMATORY DISEASE

Total number of patients	30	
Normal sedimentation rate	3	10 per cent
Abnormal sedimentation rate	27	90 per cent

TABLE II. ACUTE PELVIC INFLAMMATORY DISEASE SEDIMENTATION RATE IN ONE HOUR

RATE	PATIENTS	PER CENT
3-10 mm.	3	10.0
11-20 mm.	12	40.0
21-30 mm.	13	43.3
31-40 mm.	2	6.6

He reported quite a large number of patients with various conditions, among them being groups with appendicitis and pelvic inflammatory disease. Patients with both chronic and subacute appendicitis as well as with the acute type were noted in the appendiceal group. It was not specified whether the patients with pelvic inflammatory disease noted in his series suffered with an acute condition or exhibited chronic lesions.

In 1935 Lesser and Goldberger³ reported a large series of patients among whom were a considerable number with acute appendicitis and pelvic inflammatory disease. They studied 1,000 cases of the latter, but they did not mention the time elapsing between onset of the pain and the time when the blood was taken for examination. It was not apparent whether the diagnoses in the appendiceal group were simply based on clinical grounds or were verified by the pathologist. Their conclusions regarding the differential value of the test were as follows:

1. The sedimentation reading in cases of acute appendicitis is uniformly normal.
2. The sedimentation readings of all other acute abdominal conditions are consistently abnormal.

It has been stated by Nicholson, and Gruenfeld and others⁵ that the sedimentation rate in acute catharrhal appendicitis is always normal. This may be true if such a condition is demonstrable. Dr. Baxter L. Crawford,⁶ Director of the Pathologic Laboratories at Jefferson Hospital has stated that acute catarrhal appendicitis is rarely seen in the pathology laboratory. Usually the condition has progressed to a more advanced state before operation has been performed. Therefore it is essential that the test, to have positive value, must be applicable to those cases of appendicitis which have not ruptured or become abscessed.

Bannick, Gregg and Guernsey⁴ in a recent article on various phases of the sedimentation rate also studied a series of patients with pelvic inflammatory disease and acute appendicitis. Their conclusions are similar in some respects to those of Lesser and Goldberger. They state that over a two-year period they have not encountered a single case in which the sedimentation rate was definitely increased as a result of appendicitis, unless rupture had occurred.

The only paper published which takes into consideration the duration of pain prior to the blood being taken for examination is one by Smith, Harper and Watson⁷ who employed the Linzenmeier technique in their studies. They concluded that the rapidity of blood sedimentation was of differential value between acute appendicitis and acute pelvic inflammatory disease, if a comparatively short time had elapsed between the onset of the pain and performance of the test.

A brief description of the plan used in our investigation is indicated in order to show more clearly the precise nature of the study and its possible value.

The patients accepted for inclusion in the pelvic inflammatory group were subject to a definite diagnosis of acute pelvic inflammatory disease, based upon the following criteria:

I. History:

- a. Onset, location and duration of pain in hours, prior to performance of test.
- b. Elimination of previous attacks.
- c. Relation of onset of pain to menses.
- d. Vaginal discharge.
- e. Urinary symptoms.
- f. Exclusion of demonstrable pathology elsewhere.

II. Examination:

- a. Inspection of vulva, urethra, Skene's ducts, Bartholin's glands, and cervix with microscopic examination of discharge if present.
- b. Bimanual examination, excluding those patients with adnexal enlargements.
- c. Temperature, pulse, respiration.
- d. White blood cell count.

It might be interesting at this point to explain why we have a relatively small number of patients in the acute pelvic inflammatory group. We found that the greater proportion of patients with pelvic inflammatory disease observed in the receiving and gynecologic wards, and in the out-patient department either presented recurrent attacks, illness of longer duration than from twenty-four to seventy-two hours or definite pelvic masses. We did not accept patients with this type of pathology, since we desired to study a group closely resembling acute appendicitis in history and examination.

In selecting patients for the appendiceal group, the following criteria were required as a basis for study:

I. History:

- a. Onset, location and duration of pain in hours prior to performance of the test.
- b. Elimination of patients with histories suggestive of chronic or subacute appendicitis.

II. Examination:

- a. Abdominal and pelvic examination.
- b. Temperature, pulse and respiration.
- c. White blood cell count.

III. Operative Findings:

- a. Patients with acute appendicitis, either catarrhal, suppurative, or gangrenous, only were accepted.
- b. Elimination of patients with ruptured appendix or appendiceal abscess.
- d. Histologic examination of all removed appendices.

Patients with chronic and subacute appendicitis were not accepted because we wished to include only those with acute appendicitis verified by pathologic examination. Likewise, patients with ruptured and abscessed appendices were rejected because the longer duration of their conditions not infrequently resembles the physical signs of advanced

pelvic inflammatory disease. The plan therefore secured for study two groups of patients paralleling each other as closely in history, examination, and subsequent course as possible.

Due to the numerous methods and modifications of the sedimentation test, it is a bit difficult to convert the results of one method into those of another. The three most frequently employed methods are those of Cutler, Linzenmeier, and Westergren or a modification of one of these techniques. Regardless of the method used, the underlying principle of the sedimentation test is based on the fact that the red blood cells settle more rapidly in certain pathologic conditions than in normal individuals. Greisheimer, Treloar and Ryan⁸ made a study of the interrelation of the three methods mentioned and concluded that the average sedimentation in one hour in the case of normal individuals appears to be reasonably consistent.

Cutler's⁹ method of estimating blood sedimentation has been used in this study, since we have followed this technique routinely on the Gynecological Service for approximately ten years. The results are recorded on a chart which instantly shows the rapidity with which the blood cells settle. The procedure is as follows: Aspirate 0.5 c.c. of 3 per cent sterile sodium citrate solution into a 5 or 10 c.c. syringe. Into the same syringe draw venous blood up to the 5 c.c. mark; mix gently and force the contents into a small glass (Cutler) tube, graduated to 50 mm. Take readings every five minutes for one hour, after closing tube with a paraffin covered cork, inverting it carefully and placing it upright in a rack, certain that it is vertical and that the level of the citrated blood is exactly at the zero graduation mark. The readings are charted graphically.

Our interpretation of the test is that in healthy women the blood will sediment from within 2 to 10 mm. in one hour. When blood settles faster than 10 mm. in one hour we consider it abnormal.

Table I shows that in a series of 30 patients with acute pelvic inflammatory disease 90 per cent sedimented more rapidly than normal.

Table II shows in detail that the highest percentage of patients with acute pelvic inflammatory disease have a sedimentation rate between 11 and 40 mm. in one hour.

Table III indicates the hours elapsing between the onset of symptoms and the time that the blood was taken for the test. It will be noted that the greater percentage were taken between five and fifty hours. Only one patient had pain for 100 hours before the test was performed.

TABLE III. ACUTE PELVIC INFLAMMATORY DISEASE

LAPSE OF TIME BETWEEN ONSET OF PAIN AND RECORDING OF SEDIMENTATION RATE

HOURS	PATIENTS	PER CENT
5-25	15	50.0
26-50	11	36.6
51-75	1	3.3
76-100	3	10.0

TABLE IV. ACUTE PELVIC INFLAMMATORY DISEASE

LEUCOCYTE COUNT	PATIENTS	PER CENT
5,000-10,000	1	3.3
10,000-15,000	10	33.3
15,000-20,000	11	36.6
20,000-30,000	8	26.6

Table IV shows that in 52 per cent of the patients with acute appendicitis, the sedimentation rate was abnormal.

Table VI exhibits in detail the varying degrees of rapidity with which sedimentation took place in 52 per cent of the patients with acute appendicitis, not actually as rapid as in the acute pelvic inflammatory group (Table II) but relatively so.

Table VII shows the lapse of time between the onset of symptoms and the recording of the sedimentation rate in the patients with acute appendicitis. The similarity to Table III in the acute pelvic inflammatory group is readily noted.

Table VIII shows the grouping of leucocyte counts in the patients with acute appendicitis. Ninety-one per cent were relatively high.

TABLE V. ACUTE APPENDICITIS

Total number of patients	100	
Normal sedimentation rate	48	48 per cent
Abnormal sedimentation rate	52	52 per cent

TABLE VI. ACUTE APPENDICITIS. SEDIMENTATION RATE IN ONE HOUR

RATE	PATIENTS	PER CENT
1-10 mm.	48	48
11-15 mm.	26	26
16-20 mm.	16	16
21-25 mm.	10	10

TABLE VII. ACUTE APPENDICITIS. LAPSE OF TIME BETWEEN ONSET OF PAIN AND RECORDING OF SEDIMENTATION RATE

HOURS	PATIENTS	PER CENT
5-25	59	59
26-50	26	26
51-75	9	9
76-100	6	6

TABLE VIII. ACUTE APPENDICITIS

LEUCOCYTE COUNT	PATIENTS	PER CENT
5,000-10,000	9	9
10,000-15,000	43	43
15,000-20,000	36	36
20,000-30,000	12	12

TABLE IX. COMPARISON OF THE SEDIMENTATION RATES

SEDIMENTATION RATE	ACUTE APPENDICITIS	ACUTE PELVIC INFLAMMATORY DISEASE
Normal	48 per cent	10 per cent
Abnormal	52 per cent	90 per cent

Comparison with Table IV is especially interesting when we note that 43 per cent of the patients with acute appendicitis had a leucocyte count between 10 and 15 thousand, while 33.3 per cent of the acute inflammatory cases fell within the same limits. Thirty-six per cent of the patients with acute appendicitis had a leucocyte count between 15 and 20 thousand while 36.6 per cent of the pelvic inflammatory cases also had a leucocytosis between 15 and 20,000. This would suggest that it might be unwise to allow the leucocyte count alone to influence one in establishing a differential diagnosis.

In Table IX a comparative picture of both acute appendicitis and acute pelvic inflammatory disease in relation to the rapidity of the blood sedimentation is shown on a percentage basis.

SUMMARY AND CONCLUSIONS

1. Groups of patients with acute appendicitis and acute pelvic inflammatory disease comparable as to duration of symptoms and extent of pathology have been studied with the sedimentation test in an attempt to determine whether or not it is of value in differentiating the two conditions.

2. Ten per cent of the patients with acute pelvic inflammatory disease had a normal sedimentation rate, while 90 per cent were abnormal.

3. Forty-eight per cent of the patients with acute appendicitis had a normal sedimentation rate, while 52 per cent were abnormal.

4. We cannot agree with the reports of some observers that the sedimentation rate is never abnormal in acute appendicitis unless rupture or abscess formation has occurred; on the other hand our findings are quite in accord with those of others in regard to the sedimentation rate in acute pelvic inflammatory disease.

5. Our conclusions are that the test per se cannot alone be relied upon to differentiate between the two conditions, since in practically half of the patients suffering with acute appendicitis, sedimentation was abnormal.

REFERENCES

- (1) *Nicholson*: Laboratory Medicine, Philadelphia, 1934, Lea and Febiger, p. 45.
- (2) *Großinsky, Manuel*: Arch. Surg. 24: 660, 1932. (3) *Lesser, Albert, and Goldberger, H. A.*: Surg. Gynec. Obst. 60: p. 157, 1935. (4) *Bannick, E. G., Gregg, R. O., and Guernsey, C. M.*: J. A. M. A. 109: 1257, 1937. (5) *Gruenfeld, G., Glass, O., and Baum, F.*: J. Med. Soc. New Jersey, 1928. (6) *Crawford, Baxter L.*: Personal communication. (7) *Smith, C. T., Harper, T., and Watson, A.*: Am. J. M. Sc. 188: 383, 1935. (8) *Greisheimer, E., Treloar, A., and Ryan, M.*: Am. J. M. Sc. 187: 213, 1934. (9) *Cutler, J. W.*: Am. J. M. Sc. 171: 822, 1926.

DISCUSSION

DR. J. W. CUTLER.—For a number of years there have appeared an increasing number of papers emphasizing the necessity of correcting for anemia to make possible a more accurate evaluation of the sedimentation test. Those who hold this view believe that anemia when present materially increases the sedimentation rate so that the latter not only reflects the activity of the disease, but also the associated anemia. They also believe that one can isolate the anemia factor and correct for it by the simple procedure of subtracting sufficient plasma to bring the cell count to 5,000,000 before performing the test. The difference between the sedimentation rate of the corrected sample and the uncorrected or anemia sample would, in their opinion, represent the increased sedimentation brought about by the anemia factor itself.

In the past two and one-half years Park, Herr, and I have studied this question quite thoroughly and have come to the conclusion that anemia has little to do with the phenomenon of blood sedimentation and that one cannot correct for anemia and obtain consistent sedimentation findings. Our difficulty lies in our methods for recording sedimentation rates.

There is clinical evidence to show that marked anemia can be associated with a slow sedimentation—for instance, bleeding peptic ulcer, sickle cell and pernicious anemia. Experimentally, we can make cells, regardless of the number in suspension, sediment rapidly or slowly by adding certain substances to the plasma. If acacia

is added the cells settle rapidly, if lecithin is added, they sediment extremely slowly. The reason why some cells sediment rapidly and others slowly is not because of any difference in the size or shape or number of the cells, but whether or not they form large aggregates. If they do, they sediment rapidly, and vice versa. The ability to form large aggregates is a function of the plasma and depends on the presence in the plasma of certain substances such as globulin and fibrinogen. These substances not only have a quantitative relationship to the sedimentation rate, but also a qualitative one. Globulin, for instance, will cause more rapid sedimentation than fibrinogen. When plasma is removed, in an endeavor to correct for anemia, then the very factors responsible for sedimentation are also removed. If a large quantity of plasma is removed as is necessary when the anemia is marked, the mechanism of rouleaux formation is seriously interfered with and sedimentation may become so slow that the laboratory may report a normal sedimentation finding in the presence of clinically active disease. Those who believe in correction explain this observation as overcorrection, although the blood count of the corrected sample is 5,000,000, as in other corrected samples. This observation is not overcorrection. It is a deliberate interference with the mechanism of aggregation of red cells to the point that the sedimentation phenomenon disappears.

As a corollary of the above study, I am further convinced that our present methods for recording sedimentation rate need considerable modification. What is needed is a more scientific unit for expressing blood sedimentation, one that will express sedimentation in terms of velocity or the rate at which the aggregates settle in a given unit of time.

When such a unit will be developed, it will be independent of the size of the tube used, whether long or short, narrow or wide, since the rate of settling of the aggregates must be exactly the same in all tubes. Should such an effort be successful, then, I believe, blood sedimentation studies will take on greater clinical significance.

DR. BROOKE M. ANSPACH.—The sedimentation test gives us the most reliable signs of the degree of subsidence in pelvic inflammatory trouble. It is also a safeguard in any case, for it sometimes brings to our attention lesions other than pelvic which might exert an unfavorable influence in operative treatment. We have learned to expect a rapid rate in a secondary anemia. It has been rapid sometimes when a myoma was undergoing degeneration, and is usually so in carcinoma with ulceration and infection.

Leucocytosis is an almost immediate reaction to an acute inflammatory process, but an increase in the sedimentation rate does not begin for twenty-four to thirty-six hours. We need not be surprised with a rapid reaction in post-partal or post-abortion infections, since the sedimentation rate may have been rapid beforehand, as it is always increased in pregnancy. In the case of gonorrheal salpingitis the infection has been present in the woman for awhile before it reaches the tubes. Under these circumstances it is quite likely that the sedimentation rate has been rapid before the acute symptoms began. While we may be able in a large majority of cases to distinguish between acute appendicitis and acute gonorrheal salpingitis upon other grounds, I believe that this difference in the sedimentation rate will prove a very useful help in differential diagnosis.

THE MANAGEMENT OF BREECH DELIVERIES*

BASED ON A REPORT OF 709 CASES FROM THE PHILADELPHIA
LYING-IN HOSPITAL

ROY W. MOHLER, M.D., PHILADELPHIA, PA.

INTRODUCTION

BREECH presentations and their management in labor are problems which are interesting to all who do obstetrics. It is a well-known fact that the danger to the child who presents by the breech is much greater than to the one which presents by the vertex. Because of an appreciation of this danger in 1931 we reviewed 170 cases of breech presentations and reported them to this Society. The gross fetal and neonatal mortality was 7.9 per cent, which is about three times higher than the corrected fetal mortality for the whole group of patients delivered at the Philadelphia Lying-in Pennsylvania Hospital. Because of the original report, and the conclusions drawn from it, certain policies in the management of breech presentations were adopted. These recommendations were that all breech cases should be completely studied clinically and with x-ray, and the size of the child in relation to the size of the maternal pelvis should be considered carefully in the management of breech presentations, and that some member of the attending Staff should be present at all breech deliveries. Since the time of the original report, these recommendations have been carried out in complete detail. All breech presentations recognized during the prenatal period examinations, have had complete x-ray studies done, and measurements made according to the Ball technique. If the x-ray studies showed an unusually large baby or evidence of fetopelvic disproportion, a consultation between various members of the Staff was called, and a decision as to the type of delivery to be chosen was made.

An absolute rule for management of breeches which we think has been quite worth-while, is to have a member of the attending Staff present and ready to deliver every breech admitted to the hospital. The House Officer is given the opportunity to get experience in the management of the case, and is allowed to proceed only so long as no obstacle appears, in which case the attendant in charge proceeds with the delivery.

During the period of time extending from Jan. 1, 1930, to Oct. 1, 1937, 709 breech presentations were delivered at the Philadelphia Lying-in Pennsylvania Hospital. It was found that breech presentations occurred very frequently in premature labor, and this incidence can be explained by certain hypotheses which may be tenable. One

*Read before the Obstetrical Society of Philadelphia, December 2, 1937, in a Symposium on Breech Deliveries.

hypothesis which seems most plausible is based on the assumption that definite polarity of the child does not occur until the presenting part has become fixed in the inlet of the pelvis. It seems to me that the deaths of premature and immature infants that occur following premature breech deliveries should not be attributed to the form of delivery but to the fact that the labor was premature. If this exclusion is accepted, and if we also accept the exclusion of deformed and macerated babies, we still may anticipate a higher fetal mortality for infants delivered by breech than those delivering by vertex.

In any report on breech presentations, we must consider the fetal mortality brought about by the accidents caused by presentation and delivery as the important factor. The diagnosis of position is important, and it usually can be made without much difficulty in the patient near term. In patients with breech presentations who deliver prematurely, the diagnosis will usually be missed until labor is well advanced. For this reason, I shall confine my remarks to the management of patients with breech babies of normal vitality near term.

INCIDENCE

The incidence of breech presentation for the group of cases reported is usually 3.5 per cent. Stander in his text reports that the incidence in Schroeder's statistics was 3.11 per cent. In 50,000 deliveries at the New York Lying-in Hospital, the incidence was 3.9 per cent, and in 7,500 deliveries at the Johns Hopkins Hospital it was 3.9 per cent. The incidence at the Philadelphia Lying-in Pennsylvania Hospital, is 4.7 per cent for approximately 18,000 cases.

NOMENCLATURE

There is some confusion in the terminology applied to breech presentations. And since the type of breech one is dealing with is a factor in its management, I think I should give my understanding of the terminology used. A frank breech implies that the leg is flexed at the thigh and extended at the knee. A full breech implies that the leg is flexed at the thighs and the knees, and the term incomplete breech means that either one or both feet or knees are presenting.

In any consideration of breech deliveries, one must consider two methods of managing the patient. The first is to have the patient deliver vaginally if possible without too much danger to the child or mother. In those cases where vaginal delivery was the method chosen, the management was according to certain rules. As soon as labor was definitely established, analgesia was produced with nembutal and scopolamine, unless there was some contraindication to its use. The dose varied from 6 to 9 gr. of nembutal, and 1/100 or 1/150 gr. of scopolamine; the dose of nembutal varied somewhat according to the weight of the patient, and also because of the size of the routine dose which was being used over certain periods of time. At present, we are using 4½ to 6 gr. of nembutal with the original dose, and supplementing this dose later if necessary.

As long as labor continues it is allowed to progress until the breech or presenting part has delivered through the vaginal outlet. When necessary, just before the presenting part has delivered, gas-oxygen anesthesia is produced during the pains, and an episiotomy is done. As soon as the baby has been delivered to a point just at the umbilicus, a breech extraction is performed. Sometimes this extraction consists only in directing the body through its exit, but usually it consists in carrying out a definite technique and procedure.

TECHNIQUE OF PROCEDURE OF EXTRACTION BY VAGINA

When the breech has been delivered to the umbilicus, complete gas-oxygen anesthesia is induced. It is very important to wait for the extraction until the anesthesia is complete so that the movements of the patient do not interfere with the technique of the method chosen. With both hands the hips of the baby are grasped by the attendant, and the body of the child is rotated squarely under the arch of the symphysis. With gentle and firm traction, the body of the child is delivered until the tips of the scapulae are visible under the symphysis. During this manipulation a trained assistant locates the head of the baby through the abdominal wall and follows its descent toward the pelvis; an effort is made to keep the head flexed and the descent must be slow, being always mindful of the fact that the arms may become extended. When the scapulae show from under the symphysis pubis, the shoulders have a tendency to rotate into an anteroposterior position, and with continued gentle traction at about 135 degrees, the anterior arm will deliver either spontaneously, or with slight traction in the posterior axillar fold. After the delivery of the anterior arm, the body of the child is rotated 180 degrees through an arc in the opposite direction. This maneuver will convert the undelivered arm into an anterior arm, and it can be delivered as the first one.

After the arms have been delivered, the head is directed into the pelvis, and is manipulated into a direct anteroposterior position by firm and properly directed pressure from above, and gentle traction from below. At this point the aftercoming head forceps, as devised by Dr. Edmund Piper, are applied, with the body of the child held in an extended position above the symphysis of the mother. Great care must be exercised in this maneuver so that there is no injury to the child's body. After application of the aftercoming head forceps, the head is delivered by making traction with the forceps and combining the traction with a slight effort at flexion. No effort must be made to hurry any of these maneuvers and no strenuous force should be applied. The force used must be well distributed and directed so that it will do no injury to the child.

In those deliveries where labor does not progress normally, a decomposition and extraction of the child is done under deep surgical anesthesia, providing the cervix is completely dilated and effaced. No effort is made to deliver a baby through an undilated cervix. If de-

livery of the child is absolutely necessary before the cervix is completely dilated, an effort is made to dilate it manually, or if this is not possible or judicious, a cesarean section is performed.

In breech presentations where labor is long and progress slow with the membranes already ruptured for some time, a very serious problem confronts the attendant and each of these cases is a difficult situation which must be considered individually as it arises. It is this type of case which will always increase the fetal mortality for breech presentation unless we are able to anticipate them either before labor has begun or early in labor. Each of these difficult cases will be managed according to the individual's experience and judgment and according to the circumstances. No outline of the procedure necessary in such conditions will be touched upon except to remark that it is this type of case above all where it is certainly wise to resort to cesarean section before labor, or soon after labor has begun.

In cases when after a careful study it was learned that there was evidence of fetopelvic disproportion, or if the baby seemed larger than normal and the mother was not one with whom an undue risk should be taken, an elective cesarean section was performed.

In this group of 709 cases there were 58 cesarean sections. These patients had the sections performed after consultation with various members of the Staff and many of them had a trial of labor. Of this group of 58 cesarean sections, 40 were done because of a fetopelvic disproportion with a breech presentation, and the other 18 were done because of some accident of pregnancy in addition to a breech presentation. In this group there were 50 live babies and of the 8 babies lost, one of these was delivered from a patient where a large breech was the sole indication for the type of delivery chosen. The other 7 babies were lost because of other accidents of pregnancy, such as placenta previa, premature separation of the placenta, etc. In view of these statistics, we feel that our final decision to do a cesarean section on each of these cases was justified.

ANALYSIS OF STATISTICS

There were 709 breech presentations delivered at the Philadelphia Lying-in Pennsylvania Hospital during the period extending from Jan. 1, 1930, to Oct. 1, 1937. Of this group there were 295 primiparas and 414 multiparas. The gross fetal mortality was 186 babies, or about 26 per cent. In this group there were 49 babies from the 295 primiparas, and 98 babies from the multiparas, or a total of 147 babies that were lost because they were premature and nonviable, or deformed so that the type of presentation was not responsible for their deaths. There were 39 babies in the whole group which were lost and came under the list of corrected mortality, 18 from primiparas, and 21 from multiparas. These 39 babies represent a 5.5 per cent corrected fetal mortality for the whole group of babies presenting by the breech. This 5.5 per cent fetal mortality for breeches compares with a 2.5 per cent corrected fetal mortality for all patients delivered at the Philadelphia Lying-in Pennsylvania Hospital. The 5.5 per cent fetal mortality also compares

with a 7.9 per cent fetal mortality for breech deliveries which occurred in a series of 170 patients which were previously reported, and also compares favorably with other large series of breech deliveries, the corrected fetal mortality for which is usually near 6 per cent.

CONCLUSIONS

I have presented an outline of the points which we at the Philadelphia Lying-in Pennsylvania Hospital believe are important in the management of breech presentations.

This paper is based on 709 consecutive breech deliveries which occurred after certain policies based on an analysis of 170 breech deliveries was formulated.

The important points we feel are as follows:

1. That x-ray study should be used late in the prenatal period to determine the relative size of the fetus and mother.
2. That it is safer for the baby to deliver a larger than average sized child presenting by the breech by cesarean section.
3. That all breech babies delivered by vagina should be extracted under light anesthesia after the breech has been delivered, and this extraction should never be undertaken by anyone who has not been adequately trained with supervised experience in the management of breech deliveries.
4. That all decomposition of breech babies should be accomplished under deep surgical anesthesia after the cervix is completely dilated.
5. That aftercoming head forceps should always be used after the head has become engaged.

1806 SPRUCE STREET

DISCUSSION

DR. EDWARD A. SCHUMANN.—I am firmly convinced that in the greater number of cases the cause of breech presentation is purely accidental, that the fetus of sufficient size to be held in the pelvis is caught with the breech down by a series of intermittent uterine contractions. This is based upon a study of a series of multiparas. In a minority only breech presentation occurs because the shape of the fetus or uterus demands such presentation for the better accommodation of the fetal body in the uterine cavity.

If we were able to distinguish between the types, the whole question of external version could be more easily solved. If the position is an essential one in which the fetus fits the uterus, external version is contraindicated. Most external versions I practice are back as a vertex the next time I see the patient. Furthermore, however little pressure may be required in turning the child, there is danger of producing an abnormal cephalic presentation. The matter of cord disturbance also still impresses me seriously. I do not believe that external version is a practice I would regularly follow.

With regard to the management, I wonder why it is necessary to extract the child when the umbilicus is delivered. If the umbilicus appears, the child will continue to come down. In spite of the essayists' account of the ease with which the arm delivers itself spontaneously with slight pressure, the arm sometimes offers a great deal of difficulty. Of course, if one follows the fundus from above, the danger of extension of the arm is minimized. The main thing is to maintain flexion and the more you maintain this the simpler the breech extraction. I would prefer to push rather than pull on the breech. If I were to extract a breech, I would prefer to do the decomposition early, when the breech appears at the vulva rather than

to wait until the umbilicus comes down. Because I believe that the danger to the baby in breech is not asphyxia but intracranial traumatism, I am convinced that the longer the pelvic tissues are permitted to dilate and the oftener the baby is permitted to deliver spontaneously, the less will be the fetal mortality.

Dr. Wall, of Kensington, is presenting our own set of statistics. In that institution we practice the policy of noninterference whenever possible. Obviously, there are instances when progress is assisted, but we attempt to deliver the breech spontaneously whenever possible. As to the aftercoming head forceps, we use the instrument in all cases except where the head falls out before the forceps can be applied.

DR. NORRIS VAUX.—I do not believe in external version. I cannot see the reason for converting a breech to a vertex when nature has presented some abnormality or unusual condition in the lower uterine wall or pelvis which has caused the breech to become dependent. Furthermore if external version is done, I cannot agree with Dr. Mohler's comment on the subject, that the patient should be allowed to be ambulatory during the twenty-four hours following the procedure, because the placenta may be somewhat detached, the cord may become twisted around the child, or inadvertent rupture of the membranes may occur.

Breech presentation and delivery has its own mechanism similar to the mechanism of the vertex. If we understand this mechanism, and if the mechanism of breech is progressing normally, it is our practice to leave it alone, using analgesia, sedation and anesthesia where necessary, until the navel of the child appears. We do not assist it from there on unless the mechanism ceases to progress, and fortunately this does not often happen. The delivery is more likely to become obstructed when the shoulder girdle gets into the pelvic cavity. The remaining portion of the breech extraction or delivery, the aftercoming head, usually produces our greatest difficulty. The head must be kept flexed. The worst thing we can do is to pull on the breech that is descending, except to guide it.

We have no difficulty with what is called the decomposition, when the breech is arrested in midpelvis and the cervix is fully dilated. Extraction of an impacted breech, however, is a different consideration and is only attempted and performed under deep surgical anesthesia. Early episiotomy and aftercoming head forceps are used.

DR. ROLAND PORTER.—A small point I wish to bring out is that a fair proportion of breech cases change to vertex, especially in the multiparas with the globular uterus. That has been proved numerous times by comparing the x-ray in the dispensary and the later position when labor begins.

It is often said that after the baby is down to the umbilicus deep surgical anesthesia is desired. I keep my patients in as light anesthesia as I can so that uterine contractions keep the head and body placed.

Lacking Piper forceps, an ordinary Simpson forceps can be applied to the aftercoming head with a great deal of success in most cases.

DR. CARL HENRY DAVIS.—Some years ago I referred a multiparous patient, who had delivered easily the first time, to a younger man who was interested in external version. Finding that she had a breech presentation he attempted an external version in his office but did not succeed. Later he took her to the hospital and did an external version under ether anesthesia. Twenty-four hours later she delivered a stillborn infant which had been alive at the time the external version was performed.

In my earlier teaching experience we did not have the large clinical material which is now available, and we tried to save our breech deliveries for the students. It was, therefore, necessary for us to learn how to deliver the patient who had a breech presentation and, having learned, I, like many others, have ceased to fear the average breech delivery.

DR. WILLIAM R. NICHOLSON.—I am perfectly certain that the mortality that has been reported in breech delivery has been in most instances the result of undue interference. It is perfectly true that there are some cases of breech

delivery in which interference is necessary, but the indication in my experience has been very rare. What I have always objected to was the teaching prevalent some years ago that just as soon as the cervix in a breech labor was dilated delivery should be effected. If this teaching is followed there is every reason in the world to lose babies.

Cesarean section has a definite indication in certain cases of breech, particularly with moderate pelvic contractions, or in old primiparas in whom the probability of another child may be remote. I use external version where possible in order to determine any disproportion between the head and the pelvis. This is my only indication for external version.

I feel that we are going back to the well-established methods which years ago governed the delivery of these cases. There is one recent advance, however, namely, the use of forceps on the aftercoming head, instead of old manual procedures. In every breech delivery the forceps should be prepared ready to put on if there is any retardation in the delivery of the head.

DR. COLLIN FOULKROD.—Too much stress has I feel been laid upon the normality of breech births. It is often the younger man who will allow the labor to go to the point of danger to the child, a condition more likely to occur in breech than in vertex presentations. In breech presentations the slowing up of the process of labor must therefore be watched more carefully than in a normal vertex, and interference practiced earlier if the conditions present should warrant it.

A relaxed multiparous uterus will be flaccid up until about one month prior to labor. Then during the period of settling with increased uterine contractions a breech may change to a vertex presentation. It is better therefore to wait until after the thirty-eighth week of gestation to try external version. With the usual multipara where the measurements are normal and the knowledge you have justifies you in trying external version, it is far better to wait until near term, to do the version, and then to rupture the membranes at the same sitting, by that means keeping the head in the pelvis and starting labor.

A breech will often go longer than the computed time of maturity, perhaps because the breech does not sink into the pelvic cavity as well. For reasons of disproportion a section may therefore be necessary.

DR. GEORGE ULRICH.—It is interesting to consider the cause of infant mortality in breech presentation. If you look up statistics you will find the lowest mortality is in the babies weighing from 7 to 9 pounds. Babies born in breech presentation and weighing less than four pounds are almost all lost; between four and five pounds, two-fifths are lost; between five and six pounds, less, and between seven and nine pounds, possibly not more than one-twentieth are lost. It is not the difficulty of breech delivery that causes the infant mortality, but the pressure on the premature head.

Waiting is a good policy, but how long should we wait? There is no indication for interference so long as the mother remains in good condition, the heart sounds of the baby hold to normal, and labor progresses. The criteria for interference should be the cessation of progress. The baby will very soon show the results of this.

Years ago we were taught two ways of delivering breeches; one by expression, and the other by extraction. Many women who have almost enough uterine force to push the breech over the perineum can be delivered by making slight pressure over the fundus of the uterus. This starts the breech over the perineum, stimulates contraction of the uterus and pushes the baby out.

One thing about aftercoming head forceps that every man must remember is never to use them until the head is engaged. I have seen infants killed and mothers maimed, just because this one little thing is forgotten. Also remember that the head cannot engage until it is first flexed. Flexion may be maintained by making pressure over the fundus of the uterus during traction.

DR. ALICE TALLANT.—The point about pressure on the fundus I once saw perfectly illustrated in the Charité Hospital in Berlin. The nurse on the Ward

was a trained German midwife. On one occasion a woman in the delivery room seemed to be in active labor and the interne went to see what was happening. He saw the breech presenting and rushed for the Chief. The midwife gave one glance of scorn at the fleeing interne, placed her hand on the patient's fundus, and with one push the baby shot out upon the bed, while the nurse walked calmly on her way.

DR. JOHN C. HIRST.—In the last 3,100 deliveries at the Preston Retreat we had 124 breech deliveries resulting in 15 stillborn and 16 neonatal deaths, but we were able honestly to deduct 26 fatalities because of developmental defects, prematurity under twenty-eight weeks, and placenta previa, making a corrected mortality of 5 babies in 98 births, or slightly over 5 per cent. In the last 1,600 deliveries for which I have been responsible, we have made a real effort to do external version for each breech baby in a borderline pelvis. Among these cases we have had 53 breech presentations without a single viable death, only one decomposition and no cesarean sections.

DR. H. H. MUHLENBERG.—The country doctor may first of all emphasize the wisdom of not becoming terrified in the presence of a breech presentation, and giving the breech plenty of time, while carefully observing the fetal heart sounds. My second point is the great improvement in our statistics since we have routinely used aftercoming head forceps instead of making great pressure on the head from above.

DR. LIDA STEWART COGILL.—In a case where there is no existing disproportion between fetus and pelvis and no immediate need for delivery of the fetus, the patient should be permitted to deliver herself without any interference from the attending physician.

She may be assisted by means of the Kristeller method, which consists of placing the hands over the fundus and at the sides of the uterus, pushing downward during uterine contractions, thus aiding in the expulsion of the fetus and the preventing of extension of the upper extremities and head which so frequently follows when traction is made from below.

I think we are all agreed there is a greater amount of intracranial pressure present in an aftercoming head than in a cephalic presentation, therefore even with the use of Piper forceps we should deliver slowly in order to prevent a sudden increase in this pressure with its attending ill effects upon the fetus.

DR. ROY W. MOHLER.—May I call your attention to the fact that I said "complete" but not "deep" anesthesia. Anesthesia with gas and oxygen cannot be deep anesthesia. I also said that sometimes the extraction consists in only directing the baby through the mechanisms of labor. If you are going to anesthetize the patient you have to do something to direct the child through the pelvis in order to have a definite maneuver in labor.

DR. J. O. ARNOLD.—Dr. Mohler's report brought to mind my first and, as I look back now, most impressive lesson in the conduct of breech delivery. It was the first breech delivery I had ever seen and occurred at the Lying-In Hospital from which Dr. Mohler's report comes. The attending obstetrician and instructor, standing idly by while the child's unsupported breech protruded farther and farther with each pain, led to all kinds of wonderment on the part of the students. The attending doctor, noting our bewilderment, began to question us: "What should the attendant do now? What should be the position of his hands at this point in the conduct of the case?" When we had each attempted an answer, he said: "No, his hands should be as mine are now," and he stood apart from the delivery table, with his hands behind his back!

We have largely taught in our own clinic this hands-off, watchful-waiting policy, and from a review of our case records for a good many years, we have no reason to regret this cause. With all the improvements in methods, and the tendency to substitute artificial processes for the natural, the fact still remains that there is a decidedly higher fetal mortality with interference than without interference. It

takes a lot of experience and obstetric judgment to know when and how to interfere in the breech presentation, and the great majority of physicians doing obstetric work do not have that experience and judgment.

We have not thought well enough of the advantages of external version to practice it routinely at Temple. The more frequent use of forceps on the after-coming head and of perineotomy when there are indications of undue delay or difficulty, unquestionably are steps in the direction of lessened traumatism to the child, and therefore of lowered infant mortality. We should not lose sight of the fact, however, that more babies die from traumatism due to untimely interference, than from asphyxia from delay in delivery, or want of interference. We still believe in the wisdom of that early teaching at the Lying-In, and that, everything considered, it is safer to teach our undergraduates and internes to let the breech alone, and to keep hands off as long as possible, and wherever possible.

THE COLD PRESSOR TEST IN PREGNANCY*

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WE BEGAN to use the cold pressor test shortly after Hines and Brown described it. In a preliminary report published in 1935, we noted that pregnant individuals with a family history of hypertension usually gave more marked responses to the test than patients without such a history. Pre-eclamptic and eclamptic patients showed no uniform results with the test. Those patients who had hypertension, which was usually of the essential type, gave marked responses, both ante partum and post partum. It seemed that the test could be used to detect those patients who might subsequently in pregnancy develop hypertension or show evidence of vascular renal disease. The results of such a study are presented in this report.

Randall, Murray, and Mussey also applied the cold pressor test to pregnant patients. They found that 7 patients who were normal at the time of the test, but who gave an abnormal response, subsequently developed toxemia. They drew no conclusions but pointed out that 33 per cent of the patients who gave an abnormal test subsequently developed toxemia of pregnancy.

Briggs and Oerting, in 1937, reported their results of a study of 233 pregnant women. Only two hyperreactors were found, with no familial history of hypertension. No cases of toxemia that were of hypertensive origin occurred in the normal reactor group. Toxemia of nephritic origin did occur twice in the normal group. They concluded that their series was too small for definite conclusions, but it did seem that toxemia occurring upon a hypertensive background might be determined by means of a cold test.

TECHNIQUE

The subject is placed in a comfortable chair or in a semireclining position in bed. All extraneous noises and distractions are reduced to a minimum. A blood pressure cuff is applied to the arm and an arm band stethoscope is then adjusted to the cubital fossa.

If the patient cannot rest for an hour, blood pressure determinations are made at two- to three-minute intervals until a basal reading is obtained. The temperature of the water, which is 1° to 2° C., is obtained by having chipped ice in the water.

*Read before the Central Society for Clinical Research, November 5, 1937.

The extended hand of the arm wearing the blood pressure cuff is immersed until the ice water reaches the wrist. Blood pressure readings are taken immediately and then every thirty seconds for two minutes when the hand is removed. The blood pressure is then taken at three-minute intervals for an additional fifteen minutes to note the time required for the blood pressure to return to the normal level.

One individual has performed most of our tests. A container, measuring 9 by 16 by 10 inches high, with an inclined screen 16 inches long at one end, was found more satisfactory than a pan. Ice chips were kept behind the screen, thus maintaining the temperature of the water at 1 to 2° C.

Over 400 pregnant women have been subjected on one or more occasions to the cold pressor test. One hundred fifty-two patients who were normal in all respects at the time of the test and who did not deliver for at least three months were selected for study. Our criteria for toxemia are as follows:

A systolic blood pressure of 140 or more on more than two days.

An extensive edema of the legs or generalized moderate edema with no recognizable cause except the pregnancy.

A proteinuria which is present daily for at least one week or which is noted on repeated tests for more than four weeks. The specimen of urine must be uncontaminated and there must be no urinary tract infection.

Usually more than one of the above are present.

Our data are listed in Table I. An abnormal vascular renal system may manifest itself during pregnancy as follows:

A. A transient rise of the systolic blood pressure to 140 mm. or more for one day. Proteinuria may frequently be associated with the hypertension.

B. A coincidental essential hypertension appearing early in pregnancy and becoming more severe as the pregnancy grows.

C. The exacerbation of an essential hypertension or of a chronic glomerulonephritis.

TABLE I. COLD PRESSOR TEST IN NORMAL PREGNANT WOMEN

TRANSIENT OR PERMANENT ABNORMALITIES OF THE VASCULAR RENAL SYSTEM	INCREASE IN SYSTOLIC MM. MERCURY		
	0-19	20-29	30 OR MORE
Hypertension		2	11
Hypertension and proteinuria			4
Hypertension, proteinuria, and edema			6
Hypertension and edema	1		3
Proteinuria	2	1	2
Edema		1	2
Total cases with abnormal vascular renal pathology	3	4	28
Total cases with normal pregnancy	27	28	62
Total	30	32	90
Patients with toxemia or permanent vascular renal disease	1	1	15

These vascular renal signs must be distinguished from the typical or true toxemia of pregnancy, i.e., pre-eclampsia.

Hines and Brown, in their first report, stated that the patient was a hyperreactor if the ice water test caused an increase in the systolic pressure of more than 15 mm. Randall and co-workers in pregnant

patients took 20 as the maximal increase. Subsequently, Hines and Brown took 22 as the upper limit of normal in the nonpregnant. We have taken 29 as our upper limit of normal.

The large number of pregnant women who are hyperreactors requires consideration. We know that the blood pressure increases slightly as term is approached. The cause and mechanism are unknown. The blood and plasma volume and vascular bed are increased. The viscosity of the blood is decreased. The pulse rate is slightly increased. The nausea and vomiting, constipation, paroxysmal tachycardia, dermatographia, etc., of pregnancy are all thought to be due in part at least to sympathetic stimulation. This may also account for the high incidence of hyperreactors.

In the 0-19 group, one patient had toxemia and 2 others had normal pregnancies with the exception of the transient disturbances mentioned. Twenty-seven patients had normal pregnancies. The results in the 20 to 29 group are similar.

Fifteen patients out of 90 in the 30 and over group had definite evidence of toxemia and in 10 cases the hypertension was still present three months or longer after delivery. Thirteen patients had the transient findings listed.

It is worth noting that of the 152 patients tested, 90 gave a cold pressor rise of 30 mm. or more and 15 of these developed toxemia. Sixty-two patients gave a pressor rise of less than 30 and only 2 developed toxemia.

Four patients with a history of previous toxemia also gave a pressor rise of 30 or more but only 2 had a recurrence of toxemia.

The result of the test and subsequent symptoms and signs were compared with the total gain in weight. Certainly the majority (90 per cent) of the patients who gave a rise of 30 mm. or more, and either had toxemia or transient vascular renal symptoms, gained less than 15 kilograms of weight during pregnancy. Thus, these patients differ from those with pre-eclampsia who usually gain excessively or too rapidly or both.

Hines and Brown stress the importance of obtaining a basal blood pressure before testing the patient, and emphasize the value of comparing the "range" value with the "ceiling" value. They found that 98 per cent of the normal subjects, with normal range, had a ceiling of less than 145 mm. in the systolic pressure. Seventy-two per cent of the normal hyperreactors had a ceiling of more than 145 mm. systolic.

Several investigators have been unable to confirm the work of Hines and Brown. We believe that if basal pressures are obtained and if the blood pressures are taken every thirty to forty seconds during the immersion, certain patients will give marked increases in blood pressure and others little or no effect. Occasionally the blood pressure drops. To eliminate the personal factor, we have used the Tycos self-recording sphygmomanometer in a number of cases with results similar to those found with the auscultatory method. Furthermore, as we have previously reported, repeated ice water tests on the same day in 5 patients precipitated alarming vascular renal symptoms and signs.

Chart 1 illustrates the results of the cold pressor test on a nonpregnant woman with family history of hypertension and the blood pressure curve of this same patient during pregnancy and the puerperium. A severe toxemia which we believe was primarily an essential hypertension was caused or precipitated by the pregnancy in a patient who had a predisposition to vascular disease. The blood pressure was still abnormal almost three years post partum, and we believe that it will not only never return to normal but will slowly increase. If other pregnancies occur, the rate of increase of the pressure will be hastened. We have similar curves for 14 other patients differing only in that the test was performed during pregnancy.

We, as well as several other physicians, have used the test in nonpregnant women as an aid in deciding whether or not it would be advisable for them either to become pregnant or have more pregnancies. If the patient has a border line blood pressure, 130 to 140 systolic, and gives a rise of 30 or more with the cold test, we advise against pregnancy. If the patient gives a history of previous toxemia and also is a hyper-reactor, we believe pregnancy is contraindicated. However, if the test is normal, the patient may become pregnant.

We certainly do not believe at this time that every patient, whether pregnant or not, whose systolic pressure increases 30 mm. or more after

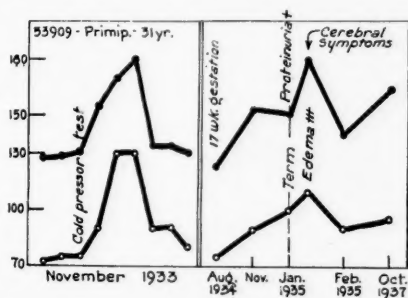


Chart 1.—Graph of cold pressor test and blood pressure curve of patient in subsequent pregnancy.

the cold test will either develop toxemia or should not become pregnant. But there is a definite relationship as indicated by our work as well as by that of the other two reports previously cited.

We have also been studying the effect of pituitrin on the blood pressure. Normal pregnant patients, after the subcutaneous injection of 1 to 2 minims of pituitrin, show an average increase in the systolic pressure of 11 mm. with a range of 0 to 20. Pre-eclamptic patients have an average increase of 51 and a range of 28 to 80 mm. Patients with essential hypertension or vascular renal disease have an average rise of 7.7 and a range of minus 10 to 18. Thus, pre-eclamptic patients give a marked response to pituitrin but a normal one to the cold pressor test. The patient with essential hypertension, with vascular renal disease or with family history of hypertension usually gives a marked response to the ice water test but a normal one to pituitrin. It seems that these tests may be used during pregnancy to differentiate the various types of toxemia and if used early in pregnancy they may indicate which patients may develop pre-eclampsia and which hypertension. At present

we are using them for differentiation of the toxemia and plan to apply both tests to a group of normal patients in early pregnancy and follow their subsequent course.

If a large number of tests confirm our findings, the cold pressor test will be of great value. First, it will enable us to select those patients who may develop toxemia and thus permit frequent observation and intensive study of these patients. The group of normal reactors need not be seen so frequently, thus decreasing the cost of prenatal care for this group. We, therefore, hope that other clinics will adopt it in order that a series of several thousand patients may be quickly collected.

SUMMARY

The cold pressor test was used in 152 normal pregnant women.

An increase in the systolic pressure of 30 mm. or more was considered abnormal.

Ninety patients were hyperreactors, 15 developed toxemia and an additional 13 had transient abnormal vascular renal signs.

Sixty-two patients gave a normal test. Only 2 developed toxemia and an additional 5 had transient signs.

The cold pressor test is compared with the pituitrin test.

An abnormal reaction of the former in a pregnant woman seems to indicate that she may develop a toxemia in which the hypertension is the predominant finding. An abnormal pituitrin reaction commonly occurs in patients with toxemia of the pre-eclamptic type.

REFERENCES

- Briggs, J., and Oertling, H.: *Minn. Med.* 20: 382, 1937. Dieckmann, Wm. J., and Michel, H. L.: *Arch. Int. Med.* 55: 420, 1935. *Idem*: *Proc. Soc. Exper. Biol. & Med.* 32: 1591, 1935. *Idem*: *AM. J. OBST. & GYNEC.* 33: 131, 1937. Hines, E., and Brown, G.: *Ann. Int. Med.* 7: 209, 1933. Randall, L., Murray, S., and Mussey, R.: *AM. J. OBST. & GYNEC.* 29: 362, 1935.

Cotte: *Surgical Treatment of Pruritus Vulvae*, *Gynéc. et obst.* 36: 257, 1937.

Among the minor surgical procedures Cotte mentions linear scarifications, superficial cauterization and local injections of anesthetic solutions or other liquids. In the latter class the best results have been obtained with injections of alcohol. Injections of oxygen and radioactive substances have also been used. Some physicians inject anesthetic solutions into the pudic nerves.

Among the more extensive surgical procedures, Cotte mentions vulvectomy. This operation is popular, but he is not impressed with its results. He discusses section of the subcutaneous and also the internal pudic nerves but personally favors resection of the presacral nerve. He performed two of these operations in men and three in women who had pruritus around the genital and anal regions. In this small series there were two complete and two partial successes and one failure. Cotte collected reports of 17 presacral nerve resections for pruritus. Of these patients 10 were completely, and 4 partially, relieved, and 3 cases were failures. The author prefers resection of the presacral nerve because it permits examination of the pelvic contents, carries little danger, and does not interfere with sexual function.

J. P. GREENHILL.

HEART DISEASE COMPLICATING PREGNANCY

A STUDY OF 436 CASES

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A STUDY of 436 women, suffering from cardiac disease and observed in 493 pregnancies in the Lying-in Hospital (Woman's Clinic of the New York Hospital) during the five-year period ending Sept. 1, 1937, is the basis for this report. In a recent publication¹ Kuder and I described the role of a special ante-partum and post-partum cardiac clinic and the manner in which cardiac patients are treated in the Lying-in Hospital. In the present analysis emphasis is directed mainly to the important role heart disease plays in maternal mortality.

During the five-year period under review, cardiac disease occurred as a complication in 493 of 14,009 pregnancies on the Indoor Service of the Lying-in Hospital, an incidence of 3.5 per cent.

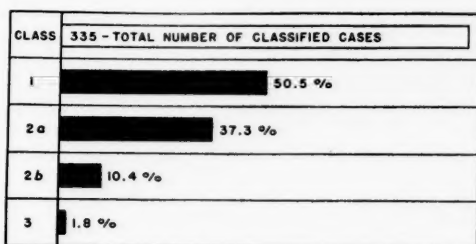


Chart 1.—Distribution of heart disease according to functional classification.

As stated elsewhere² we employ the functional classification of heart disease, formulated by the New York Heart Association. In 335 of the 436 patients studied, there was full agreement as to the exact classification, and we, therefore, believe that an analysis of this smaller group would be more accurate as to the relative frequency of the various classes of heart disease. In these 335 patients the distribution, according to the functional classification, is shown in Chart 1, which reveals 50.5 per cent of the cases of Class I, 37.3 per cent in Class IIa, 10.4 per cent in Class IIb, and 1.8 per cent in Class III. In other words, half of the patients belong in the mild Class I, whereas the other half fall in the potentially or actually dangerous groups (Classes IIa, IIb, and III).

In order to portray our attitude as to the value of early hospitalization prior to delivery in the several grades of heart disease, Chart 2

*Read at a meeting of the New York Obstetrical Society, December 14, 1937.

has been prepared. Whereas the Class I patients averaged only slightly over one day in the hospital prior to delivery, the severe Class III patients averaged 51.5 days. Although we have, of course, no rule or standard routine regarding the period of hospitalization, the figures in Chart 2 show almost a geometric progression, dependent on the grade of heart involvement.

Not only is it necessary that heart disease, if present, be recognized before or very early in a pregnancy, and adequate rest and hospitali-

CLASS	335 - TOTAL NUMBER OF CLASSIFIED CASES
1	1.4 DAYS
2 a	5.6 DAYS
2 b	17.2 DAYS
3	51.5 DAYS

Chart 2.—Average duration of hospitalization prior to delivery.

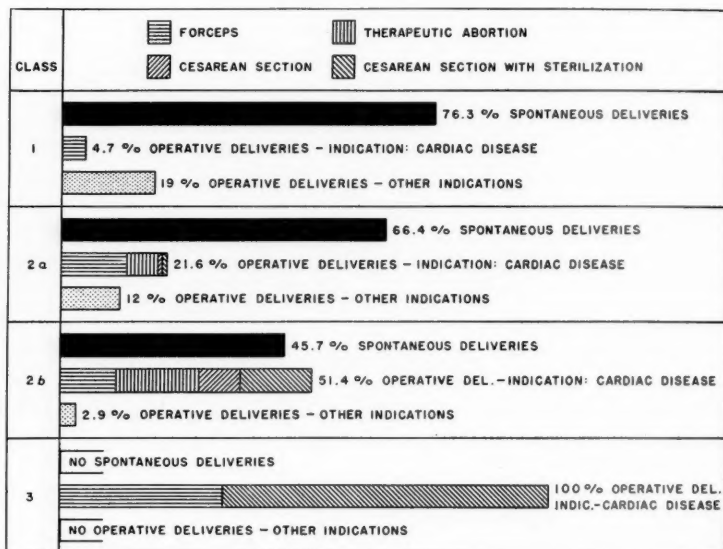


Chart 3.—Type of delivery in the various classes of cardiac disease.

zation during pregnancy be instituted but it is equally important that the patient receive the proper attention and treatment during parturition. We have found it exceedingly difficult, if not impossible, to follow any rule or routine. In Chart 3 an attempt is made to present a comprehensive view of our treatment during the delivery period. In each Class of cardiac patients, the types of delivery are divided in three groups, spontaneous, operative because of heart disease and operative on indications other than heart disease. Four further subdivisions of operative deliveries are shown, viz., forceps, therapeutic

abortion, cesarean section, and cesarean section with sterilization. Spontaneous delivery occurred in 76.3 per cent of Class I, 66.4 per cent of Class IIa, 45.7 per cent of Class IIb, and zero per cent of Class III cardiac patients. On the other hand, the operative deliveries performed because of heart disease form 4.7, 21.6, 51.4, and 100 per cent, respectively, in the four classes. The third set of figures, namely those for operative deliveries on indications other than cardiac disease, are inserted to complete the figures and so enable one to compute the correct percentages for the several groups. Although, as stated above, no rule of treatment is followed in our clinic, it is noteworthy how the number of operative deliveries, because of heart disease, proceeds from 4.7 per cent in Class I to 100 per cent in Class III.

Therapeutic abortion for heart disease was done in only Classes IIa and IIb. That this operation was not performed in Classes I and III, is presumably due to the fact that in the former the heart affection was not deemed sufficient reason for interruption of a pregnancy, while in the latter the patients were too ill or too far advanced in pregnancy to make interruption the procedure of choice.

It will be noted that whenever cesarean section was performed in Class III cardiac patients it was on the cardiac indication and was always accompanied by sterilization. On the other hand, cesarean section constituted only about half of the operations, based on cardiac indication, in Class IIb, and again, in only slightly over half of these cesarean sections was sterilization performed. Expressed differently, pregnant patients with cardiac decompensation or Class III heart disease complication are invariably treated with long periods of hospitalization followed by forceps delivery or cesarean section and sterilization; while those with Class IIb heart disease are similarly hospitalized, but usually for shorter periods, and are delivered either by forceps or cesarean section, with or without sterilization. It must, of course, be evident that the decision as to type of delivery, as well as to the question of sterilization, rests on many factors and is an individual matter in each patient.

It is our very definite conclusion¹ that pregnancy is a strain on the heart and that labor adds still more to this load; furthermore, that where the heart is already diseased, this strain of pregnancy and labor may be sufficient to either markedly aggravate the cardiac condition or produce actual failure resulting in death. Analysis of the maternal mortality in the Lying-in Hospital has brought this conclusion particularly to our attention. In Chart 4 are given the causes of our maternal mortality. During the five-year period studied we had 46 maternal deaths in 20,957 obstetric discharges, an uncorrected mortality of 2.18 per 1,000 obstetric discharges. This incidence may be expressed as 2.62 per 1,000 full-term and premature deliveries, or 2.69 per 1,000 live births or 2.43 per 1,000 pregnancies. We believe, as stated in an earlier publication,³ that the last figure is the most accurate expression of maternal mortality, as it takes into account abortions, ectopic pregnancies and patients dying undelivered and is not vitiated by multiple births. The method of expressing maternal

deaths on a basis of live births may be of use where full statistical data are not available, but is decidedly inaccurate as it is affected by the incidence of twins or other types of multiple births and actually utilizes the fetal mortality rate to express maternal mortality.

Approximately one-fourth of our deaths were due to hemorrhage (ante partum and post partum), and 15 per cent were due to infections. Pneumonia accounted for 13.2 per cent, while cardiac disease is the fourth most important cause of maternal mortality, accounting for 8.7 per cent of the deaths, and followed by toxemias with only 6.5 per cent. Furthermore, it is to be noted that the 3 maternal deaths, or 6.5 per cent of the maternal mortality, due to toxemias, were all caused by acute yellow atrophy and chronic nephritis. In this chart, therefore, infection is no longer the major cause of maternal mortality and the toxemias account for a relatively small percentage of the death rate, and even then it is necessary to include under "tox-

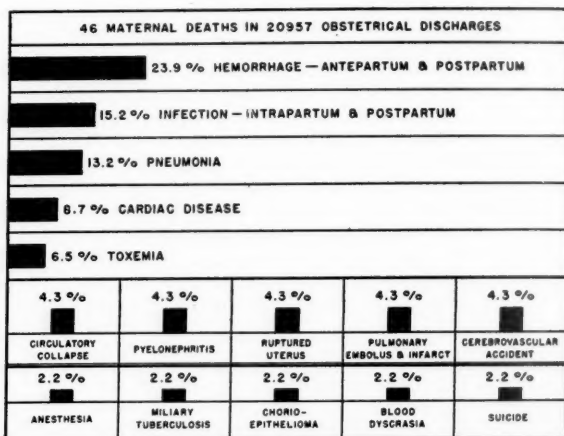


Chart 4.—The causes of maternal mortality.

emia," chronic nephritis. I have elsewhere⁴ discussed in detail the factors responsible for the reduction in maternal mortality in both these groups, infection and toxemia. Here I wish to emphasize the important roles played by pneumonia and cardiac disease as factors in maternal mortality. Hemorrhage, both ante partum and post partum, is receiving particular attention in many maternity hospitals and in our clinic by Pastore and his co-workers, who are studying the problem of blood loss in relation to infection and the toxemias.

To repeat, cardiac disease, as shown in Chart 4, is the fourth most important cause of our maternal deaths and is a greater factor, in the total maternal death rate, than the toxemias of pregnancy.

Of the 493 pregnancies complicated by cardiac disease, 475 occurred in registered and 18 in unregistered patients. Chart 5 shows that in each of the two groups, registered and unregistered, there were two maternal deaths, giving a death rate of 0.42 per cent in the registered and 11.11 per cent in the unregistered patients. It will be noted that

the maternal mortality in the unregistered patients is over 26 times that in the registered group. Although other factors come into play, such as the fact that seriously ill patients are generally brought to a hospital, the difference in these rates is exceedingly striking, and bespeaks the value of early recognition of the disease and proper hospitalization.

What is the effect on fetal mortality of heart disease in the mother? In Chart 6 we have compared the total product of conception loss in our cardiac patients admitted to the Lying-in Hospital during the

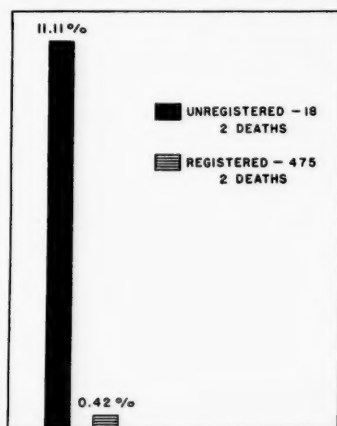


Chart 5.—Maternal mortality in registered and unregistered patients.

CARDIAC PATIENTS			
INFANTILE MORTALITY	A B O R T I O N S		11.64 %
	NON-THERAPEUTIC	THERAPEUTIC	
3.71 %	5.38 %	2.55 %	
INFANTILE MORTALITY	A B O R T I O N S		10.37 %
	NON-THERAPEUTIC	THER.	
4.12 %	5.46 %	.79 %	
TOTAL CLINIC PATIENTS			

Chart 6.—Incidence of infantile mortality and abortion in cardiac disease.

five-year period. This loss in offsprings is composed of abortions, both spontaneous and induced, whether criminal or therapeutic, and infantile mortality. Again infantile mortality includes premature, full-term, and neonatal deaths occurring within two weeks after delivery. The percentage loss in each group is calculated on the basis of the total possible live babies, which include all pregnancies, whatever the duration, as well as the multiple births. On such a basis the total offspring loss in the cardiac group is 11.64 per cent compared with 10.37 per cent in the clinic population. These totals, when analyzed further, show a therapeutic abortion loss of 2.55 in cardiac and 0.79 per cent in clinic patients, nontherapeutic abortion loss of

5.38 in cardiac and 5.46 in clinic patients, and an infantile mortality of 3.71 per cent in cardiac and 4.12 in the total clinic patient group. From these figures we may conclude that cardiac disease in the mother does not increase the loss in offspring by increasing either the rate of spontaneous abortion or infantile mortality. The only way in which cardiac disease may effect infant loss would be indirectly, through the number of therapeutic abortions performed because of heart disease.

In conclusion, I wish to emphasize the value and need of a special cardiac clinic in every obstetric service, the necessity of an adequate workable classification of heart disease, such as the functional one of the New York Heart Association, the urgent need of early registration, with a doctor or clinic, of every woman who becomes pregnant, the importance of a thorough heart examination at this first registration, the value of rest and hospitalization for patients suffering from heart disease and the importance of the proper method of delivery for each patient.

CONCLUSIONS

1. In a five-year study, comprising 20,957 obstetric discharges, from our indoor and outdoor services, the incidence of heart disease was 3.5 per cent of the total number of pregnancies.

2. The distribution of the cardiac patients, according to the functional classification, was 50.5 per cent in Class I, 37.3 per cent in Class IIa, 10.4 per cent in Class IIb, and 1.8 per cent in Class III.

3. The duration of hospitalization, prior to delivery averaged 1.4 days for Class I, 5.6 for Class IIa, 17.2 for Class IIb, and 51.5 days for Class III patients.

4. In addition to rest and long periods of hospitalization, the treatment as to delivery is most important.

5. Therapeutic abortion for heart disease was performed in only Classes IIa and IIb patients, and amounted to 2.55 per cent.

6. Forceps delivery upon full dilatation of the cervix is a great aid in the handling of many cardiac patients. This means of delivery, because of heart disease, was performed in 4.7 per cent of Class I patients, 13.6 in Class IIa, 11.42 in Class IIb, and 33.3 in Class III.

7. Cesarean section, under proper anesthesia, preferably open drop ether or local, has a definite role in the treatment of heart disease. In our series of cases cesarean section, on the indication of heart disease was performed in 1.6 per cent of Class IIa, 22.9 of Class IIb, and 66.7 per cent of Class III patients. In Class IIa about 50 per cent of the cesarean section operations were accompanied by sterilization, in Class IIb patients 62.5 per cent and in Class III patients 100 per cent of the cesarean sections were followed by tubal sterilization.

8. During the five-year period, our total uncorrected maternal mortality in the 20,957 obstetric discharges from the indoor and outdoor services was 2.19 per 1,000 discharges, or 2.62 per 1,000 deliveries, or 2.43 per 1,000 pregnancies or 2.69 per 1,000 live births. The method of expressing mortality, on the basis of the number of maternal deaths per 1,000 women who become pregnant, appears to us to be the only

accurate one, as it includes all pregnancies, of whatever duration, and does not utilize other variables, such as fetal death rate or the incidence of multiple pregnancies.

9. Cardiac disease was responsible for 8.7 per cent of our total uncorrected maternal mortality, being the fourth largest factor in this death rate.

10. The maternal mortality in unregistered cardiac patients was 26 times that in those who registered in our clinic during the prenatal period.

11. Cardiac disease in the mother does not directly effect the loss in offsprings by increasing the spontaneous abortion rate, and/or the infantile mortality rate, comprising premature, full-term and neonatal deaths. This offspring loss, nontherapeutic abortions plus infantile deaths, was 9.09 in our cardiac patients and 9.58 in our total clinic population.

12. The early recognition of heart disease, rest and long periods of hospitalization, special cardiac clinics in maternity services and the proper type of delivery are among the important factors to reduce maternal mortality caused by cardiac disease.

REFERENCES

- (1) *Stander, H. J., and Kuder, Katherine*: J. A. M. A. **108**: 2092, 1937. (2) *Stander, H. J.*: AM. J. OBST. & GYN. **27**: 528, 1934. (3) *Idem*: Ibid. **28**: 421, 1934. (4) *Idem*: Am. J. Surg. **29**: 218, 1935.

THE PROBLEM OF INFANT MORTALITY*

JOSHUA RONSCHEIM, M.D., BROOKLYN, N. Y.

FOR some time tremendous effort has been put forth in this and other civilized countries for the purpose of reducing deaths in childbirth. National, state, and local societies have organized special groups to spread the gospel of prenatal care and better care for the mother in labor and in the puerperium. A wealth of literature has been devoted to the subject, some of which has been quoted in the newspapers, firing the imagination of the public. The doctors of any given community have been literally hounded by these special groups seeking to spur them to greater effort for better care with but one object in mind—to bring the death rate in childbirth to an irreducible minimum. Throughout this entire campaign little has been said or done in an attempt to improve the possibilities for the unborn and newborn babies; they have virtually become medicine's "forgotten men." I am not unmindful of the fact that the maternal death rate for the entire country is high; I do know, however, that in the larger maternity clinics it rarely exceeds two per thousand. While we are greatly perturbed by the knowledge that, even in the best institutions, one woman in every five hundred will sacrifice

*Read at a meeting of the Brooklyn Gynecological Society, March 4, 1938, by Dr. William Epstein, Resident obstetrician, Jewish Hospital.

her life as the direct outcome of childbirth, yet we shrug our shoulders in smug complacency as the unborn and newborn infants run up a mortality of 42 per thousand or 21 times that of the mother. To me it seems a sad commentary on our obstetric teaching and practice when we must admit that 1 out of every 10 pregnancies will result in a failure; that 1 woman out of every 38 who passes the period of viability will have a dead born baby; that 1 woman out of every 68 will give birth to a live baby only to see it die during the first two weeks of its life, and, combining both the stillbirths and neonatal deaths, that every woman who passes the period of viability has 1 chance in 24 of being discharged from the hospital without her baby.

In 1918 Edgar, in a review of 519 stillbirths, pointed out that the great lesson to be learned from such a study was the necessity for adequate prenatal care. In addition he found that prolonged labor, especially when associated with dystocia, also toxemia, eclampsia, and syphilis all took their toll of infant life and could be avoided if recognized early and treated properly. He pointed out, as Bundesen and his associates have done recently, the necessity of a complete autopsy study in dealing with the question of stillbirth and regarded the premature baby as a hopeless problem.

At the end of the same year Davis, in his address before the American Association for the Study and Prevention of Infant Mortality, said "When the world is passing through a crisis of reorganization and nations are torn down and built anew, the individual fiber of a nation becomes of the greatest importance. The real test of strength is now to be made, and whatever balance may be achieved, the preservation of that balance and the hopes of the world will depend on the individual citizens of each state. The coming generation then will decide the power and pulse of this nation in the great international competition which is inevitable. More than ever are the life and health of the infant of today the insurance and guarantee of national strength for the coming generation." With the uncertain condition of world affairs today and the decline in our birth rate, it seems of utmost importance for us to recognize that these words are equally as prophetic today as they were at the close of the great war twenty years ago.

During the three years 1934 to 1936 inclusive, 6,844 pregnancies were terminated on the Obstetric Service of the Jewish Hospital of Brooklyn. The end results are shown in Table I.

TABLE I

Mothers delivered	6,844
Twin pregnancy	79
Triplet pregnancy (1)	2
Total possible babies	6,925
Abortions	309
Viable babies	6,616
Stillbirths	175
Live births	6,441
Neonatal deaths	97
Discharged live babies	6,344

Between the number of mothers admitted and the number of live babies discharged, there is a difference of exactly 500; allowing for multiple pregnancies this means that more than 500 mothers left the hospital after having been pregnant for periods varying from its inception to term with nothing to show for the suffering entailed by the pregnancy and labor. Who can measure the mental anguish endured by these women or the pelvic disorders and sterility that follow in the wake of poorly timed and badly performed operative deliveries?

A comparative study of the results obtained in several other institutions during the same three years is shown in Table II.

TABLE II

	JEWISH	HAGUE	SLOANE	LICH	LYING-IN
Abortions	4.46%	2.53%	7.55%	2.85%	6.61%
Stillbirths	2.53	2.38	1.59	2.55	2.42
Neonatal deaths	1.40	2.65	2.01	1.39	1.48
Total	8.39	7.56	11.15	6.79	10.51
Total stillbirth and neonatal death	3.93	5.03	3.60	3.94	3.90
Total cases	6,844	15,895	7,405	3,887	8,512

We observe a marked difference in the percentages of abortions and a striking similarity in the percentages of stillbirths and neonatal deaths despite the great differences in the totals of cases handled. The larger percentage of neonatal deaths at one institution probably will be explained by the inclusion in this group of nonviable pregnancies that have lived for a short time. It is my custom to classify every pregnancy which terminates before the twenty-eighth week of intrauterine life or which results in a fetus of less than 1,320 gm. as an abortion.

In an attempt to arrive at some idea as to what proportion of these babies might be saved, the abortions, stillbirths, and neonatal deaths were tabulated according to cause. Naturally, not all these pregnancies can be saved; in spite of all our efforts in this direction we will still have to face the problem of induced abortion; we probably will never solve the enigma of congenital malformation and congenital disease of hidden origin, while some of our premature infants will continue to die in spite of our best efforts to save them.

ABORTIONS

Spontaneous and induced	249
Therapeutic	43
Missed	17

While it is probable that some of the spontaneous and missed abortions will be saved by hormone and other therapy and that more careful study of some cases will result in the lowering of the number of therapeutic abortions, we are, nevertheless, in no position to make any definite statement as to how many of these could have been avoided. Prevention of spontaneous abortion may very likely lead to an increase of missed abortions. The field for prevention of infant mortality lies almost exclusively among the viable infants.

TABLE III

STILLBIRTHS		DEAD ON ADMISSION	
Dead on admission	75	Cause undetermined	37
Died before delivery in hospital	8	Maternal nephritis	4
Died in first stage labor	58	Placenta previa	1
Died in second stage labor	34	Syphilis	7
		One of twins	1
		Postmaturity	1
		Maternal cardiac	1
		Ablatio placentae	10
		Monstrosity	2
		Toxemia	8
		Prolapsed cord	1
		Strangulation of cord	1
		Trauma	1

All of these cases were carefully studied; yet in half of them we were unable to arrive at any cause of death either in the mother or in the fetus. As a great many of these fetuses are thoroughly autolyzed, necropsy is of no value other than the gross examination, microscopic investigation being impossible. Nevertheless and in spite of the difficulties that we may encounter, I believe it is safe to say that had these patients had proper prenatal care, probably more than half could have been carried to a successful issue. Syphilis, nephritis, and toxemia are alone responsible for 25 per cent of all the above stillborn babies.

Eight cases of a large number admitted to the hospital for observation and treatment in the ante-partum period suffered death of the fetus in utero. Six of these had toxemia of pregnancy, one had chronic nephritis, and one had a sudden ablatio. It is difficult to judge these cases. Premature babies of such mothers are usually poor risks, yet with proper prenatal care the outlook might have been better. Had induction of labor been performed before the death of the fetus occurred, the end result might very likely have been the same. However, the number of cases is too small to be an important factor.

TABLE IV

DEATH IN FIRST STAGE OF LABOR		DEATH IN SECOND STAGE OF LABOR		NEONATAL DEATH	
Prolonged first stage	17	Birth trauma	15	Prematurity	41
Undetermined	10	Prolonged second stage	5	Birth trauma	18
Monstrosity	6	Monstrosity	5	Monstrosity	15
Prolapsed cord	6	Prolapsed cord	4	Congenital disease	12
Ablatio placentae	5	Prematurity	2	Septicemia	4
Maternal nephritis	3	Placenta previa	2	Hemorrhagic disease	2
Eclampsia	3	Erythroblastosis	1	Pneumonia	1
Toxemia	2			Umbilical hemorrhage	1
True knot in cord	2		34	Erysipelas	1
Oligohydramnios	1			Undetermined	2
Placenta previa	1				
Prematurity	1				97
Amniotic infection	1				
	58				

It is in this large group of stillbirths and neonatal deaths, and especially among the stillbirths occurring during labor, that the field of

prevention broadens out. The deaths from birth trauma and prolonged labor constitute 30 per cent of the total and are definitely avoidable; they stand as a serious blot on our obstetric record. Many premature babies will be given a better chance if the rigid perineum is incised thus avoiding prolonged pressure on a soft head. However, we must not permit the dissemination of the idea that infant mortality can be eliminated completely. Nor should all of this mortality be placed on the obstetrician's threshold. Many abortions are self-induced and, no matter what we may do, some pregnant women will continue to disregard prenatal care even when confronted with threatening symptoms. Therapeutic abortion must be done occasionally; congenital malformation will continue to take its toll, and premature babies will sometimes fail to make the grade. Finally, we must never lose sight of the fact that every now and then the baby must be sacrificed so that the mother may live.

Investigation of the necropsy protocols reveals the fact that 168 of these 272 deaths (61.7 per cent) found their way to the autopsy table; of these only 65 gave positive information as to the cause of death. In the group which gave negative findings, there are included those whose mothers had complications such as toxemia, ablatio placentae, placenta previa, etc., also many premature infants. Then, too, many macerated fetuses had undergone such autolysis that microscopic evidence of any value could not be obtained although, grossly, nothing was found to explain the death.

TABLE V. NECROPSY RESULTS

Negative findings	103
Intracranial hemorrhage	24
Monstrosity	16
Syphilis	7
Erythroblastosis	5
Hemorrhagic disease	4
Aspiration asphyxia	4
Pneumonia	2
Rupture of trachea	1
Hemorrhage from cord	1
Pemphigus	1

What, then, can we as obstetricians do toward bringing this infant mortality to an irreducible minimum? To my mind our efforts must be directed along the following lines:

1. *Terminology.*—The question of what constitutes a stillbirth, a live birth, and a neonatal death is, apparently, a matter of choice for any given community, as a glance at the map in the article by Williams will show. Right here in New York City our Department of Health demands a stillbirth certificate for every pregnancy that does not produce a live child irrespective of the duration of the intrauterine gestation period. Likewise, every fetus that has given evidence of being alive at birth must be reported as a live birth and neonatal death, also irrespective of viability. I am quite satisfied that there must be very definite reasons for all this, yet it is obvious that such statistics only give a distorted picture because they include early and late abortions among the stillbirths and neonatal death figures. In this study all pregnancies that

terminated before the twenty-eighth week of intrauterine gestation and resulted in a fetus of less than 1,320 gm. was classified as an early abortion (if before the fifteenth week) or a late abortion. A baby born between the twenty-eighth and thirty-eighth weeks and weighing up to 2,400 gm. was classified as a premature infant; all others were classified as full term. In doubtful cases the length of the fetus was considered. If the baby weighed over 4,400 gm. and the intrauterine gestation period was over forty-three weeks, the baby should be included in the group of postmaturity. This method of grouping follows rather closely that promulgated by Adair.

2. *The Teaching and Performing of Better Obstetrics.*—It is not enough that the student and intern learn normal obstetrics; he must be taught to recognize the deviations from the normal and then, if he regard himself as not capable of dealing with the abnormality, his immediate concern should be the presence of competent assistance. Hospitals in which obstetrics is practiced should have a capable obstetrician available at all times for the guidance of those dealing with abnormalities. Those institutions with sufficient clinical material should maintain a resident staff, thus providing the competent obstetricians of the future. When labor is prolonged or dystocia is present consultation should be imperative; in this way unnecessary or wrong interference and unnecessary delay in the performing of operative delivery may be prevented. In spite of everything that we may attempt along the lines of prevention the untrained attendant will ever undertake that which he is incompetent to do; this problem will only be solved when the hospital authorities demand proof of a man's obstetric ability ere he be permitted to practice obstetrics in the institution.

3. *The Economic Problem.*—Until we make it possible for marriage to occur at an earlier age or, being married, make it possible for the young couple to have the first baby at an early period in the marriage, the elderly primipara will continue to be a source of danger. Some interesting facts are brought to light when we divide the patients into private and general service groups. Less than 3 per cent of all private patients have their first baby before passing the twentieth year; among the general service patients the figure jumps to 31 per cent. Only 5 per cent of the general service patients have their first baby after the thirtieth year as compared to 12 per cent for the private patients. *ALL* the patients who gave birth to the first baby after thirty-five years of age were private patients. If bringing forth children late in life predisposes to the possibility of monstrosity, it is plain that this source of infant mortality will be reduced if childbearing occurs in earlier life; at the same time the dangers to the baby from increased size, rigid maternal soft parts, and toxemia will be reduced.

4. *Prenatal Care.*—The importance of prenatal care must be brought home to those who do not seek it and better prenatal care must be given to those who do seek it. It is not enough that the patient be seen at stated intervals; careful interrogation and thorough investigation will frequently disclose conditions which threaten the unborn child. Syphilis,

toxemia, nephritis, diabetes, and disproportion will continue their high percentage of ante-partum and intra-partum fetal death unless we avail ourselves of the assistance of those individuals who have special training to offer. Special clinics within the prenatal clinic will safeguard the lives of many unborn children. At these special clinics the cardiologist, roentgenologist, syphilographer and others will give their advice and counsel to the obstetrician. Social service workers, visiting nurses, and maternity centers should cooperate in getting the patients to the prenatal clinics and in looking after the families while the mothers are in the hospital.

5. *Immediate and Late Puerperal Care.*—Even though there be no bleeding during labor or immediately thereafter, inspection of the cervix will frequently reveal extensive laceration which should be repaired. Proper exercises in the lying-in period will aid the involution of the uterus and help to prevent the retroversion and endometritis resulting therefrom. Later, cervical erosions should be destroyed. By these means many subsequent abortions and some cases of placenta previa will undoubtedly be avoided.

6. *The Care of the Newborn.*—Many premature infants can be saved by proper handling and feeding. Hemorrhagic disease of the newborn will become a memory when we recognize the value of injections of whole blood at the time of birth in those infants that show any cyanosis. The early diagnosis and treatment of erythroblastosis and congenital syphilis are essential if we wish to save those so afflicted. Last, mortality from birth trauma will be reduced tremendously just as soon as the practice of obstetrics is placed on a proper basis.

205 HICKS STREET

DISCUSSION

DR. WILLIAM SIDNEY SMITH.—A recent article in *Harper's Magazine*, entitled "Shall We Subsidize Our Children?" takes the view that parents on both sides of the house should subsidize their children in order that they might be able to marry young and bring forth children early. The author of this article and Dr. Ronsheim have many economic ideas in common.

I also was interested in the topic of who should care for the newborn infant, the pediatrician or the obstetrician. I have a strong feeling that the mother and the baby should be treated as an entity. The pediatrician can teach us much about the care of the newborn babe and the obstetrician can certainly teach the pediatrician much about the mother's condition, and about her labor. The care of mother and baby will be very much better if the pediatrician and the obstetrician work hand in hand.

DR. FREDERICK J. MAISEL.—I did not notice a separate tabulation of breech stillbirths in Dr. Ronsheim's tables. We recently studied our stillbirths at St. John's Hospital and while our general stillbirth incidence was comparable to that in Dr. Ronsheim's report, there was a high proportion of stillbirths due to breech presentation.

DR. JACQUES LISWOOD.—At the Israel-Zion Hospital we formerly had the pediatric staff see only service cases. We were amazed to discover that many of those service babies seemed to do better than some of the private cases. At the present time the pediatric staff goes into the nursery every morning to see if the nurse in charge reports any babies with abnormalities.

DR. GEORGE H. DAVIS.—It seems to me that neonatal care offers the greatest possibilities for reducing infant mortality. In the Hospital in which I work we have been able materially to reduce our neonatal deaths by turning our babies, private as well as ward, over to the pediatric department at birth. It may be questioned whether the pediatrician is properly trained to take care of newborn babies. His basic training, however, equips him to acquire the additional experience necessary for newborn care very quickly. Certainly in our institution his care of the newborn, particularly in premature and immature babies, has been more thorough and superior to the care given by the busy obstetrician.

DR. HARRY W. MAYES.—In our great enthusiasm to reduce maternal mortality and to check up so carefully on each death, we have seriously neglected the newborn infant. When we consider that 95 per cent of all the babies born in our city hospitals, and about 50 per cent of those delivered in the private hospitals, are under the care of residents, interns, and students, and when we realize that these cases are supervised by the attending staff only when some abnormality is noted, then perhaps we should be encouraged when we find that we have a fetal mortality of only 50 or 60 per thousand births.

Cesarean sections, versions, and forceps deliveries done with little or no indication by the untrained attendant, take their toll among the babies as well as the mothers. This may be used as one argument in favor of the midwife. The promiscuous use of drugs in the induction of labor and of analgesics and anesthetics during labor and delivery, while useful in the hand of the experienced obstetrician, may be abused by the overenthusiastic intern or resident.

I am still old fashioned enough to believe also that the mother's milk was made for the baby and that the milk contains some ingredients whether they be hormones, antitoxins, or what-not, which are vitally essential in protecting the baby from infection and preparing its alimentary canal for the functions required of it. If the baby is never taken to the mother's breast, but fed only from sterilized bottles with sterilized formulas, how is it going to establish the proper intestinal flora which is so essential in the processes of digestion? Breast feeding is a definite aid in getting the baby through those hazardous first few weeks of life.

DR. WILLIAM EPSTEIN.—In answer to Dr. Maisel's question, I may say that the types of delivery have not been separately tabulated by Dr. Ronsheim, the infant deaths due to breech delivery being included under birth trauma.

Kenny, Meave: Remote Effects of Puerperal Sepsis, Lancet 1: 14, 1937.

This study evaluates the remote ill effects of puerperal infection in 100 unselected women. An allowance was made for the psychic factors resulting from the stress and strain of pregnancy, labor and return home to the old routine with new responsibilities and the influence of the rest, care, and better living conditions of the hospital where these patients were treated.

The five groups investigated and their respective totals are: acute septic endometritis without complications, 22; pelvic cellulitis with or without thrombosis, 36; peritonitis, 14; septicemia, 19; and endometritis with complications elsewhere, 9.

The following summaries include the salient features found: Some psychical and physical debility is a common postnatal finding for those of low economic level. Complete restoration to normal health may be expected for a large majority recovering from severe puerperal infection. Rheumatoid arthritis and mitral valvular disease and some other morbid conditions appear to be closely related to puerperal infection.

Sterility is a prominent sequel to puerperal infection.

A notable number of cases revealed no gross lesion of the pelvic organs. Only 13 of the 100 women had tubal masses, uterine displacements, cervicitis, or vaginitis.

H. CLOSE HESSELTINE.

INFANT MORTALITY AT THE COOK COUNTY HOSPITAL AMONG SIXTEEN THOUSAND DELIVERIES*

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IN THE past twenty-five years, there has been a definite improvement in the death rate of infants during the first year of life. The mortality at birth and during the neonatal period has remained practically unchanged. As a result of improved prenatal care and supervision some reduction in the neonatal death rate has been achieved. There are still many intrapartum and neonatal deaths due to ill-timed, ill-chosen, and unnecessary operative procedures. Unfortunately there has been in the recent literature an indication of a tendency* in the direction of more active operative interference in labor, the wisdom of which can be seriously called into question. A statistical survey of the infant mortality at the Cook County Hospital was made to analyze the results of what may be regarded as a conservative policy in this department with respect to operative procedures including delivery by cesarean section. True conservatism consists as much in the performance of operations properly selected and performed as it does in a well-considered policy of allowing the patient to deliver spontaneously. In a study of infant mortality the question as to whether too many or too few operative deliveries are performed can only be answered by a consideration of the number of infants lost who could have been saved by some operative procedure without undue risk to the mother.

Normal deliveries are conducted by the internes under the supervision of the resident physician. Analgesias are rarely used because of the expense involved and the limitation of personnel. Inhalation anesthesia is used only when operative procedures require it. Local infiltration with $\frac{1}{2}$ per cent novocaine is used for the performance of episiotomy and repair of lacerations. Frequently, in selected cases, prudential nerve block is resorted to, for the performance of simple operative procedures.

As in all large charity institutions, Cook County Hospital accepts patients who have had no prenatal care; patients who have been referred from clinics other than that associated with the Hospital, because of complications of pregnancy or labor; and many patients who have been under the care of private physicians or midwives and are admitted to the Hospital as emergencies.

This survey covers a four-year period, 1933 to 1936 inclusive, during which time 16,242 babies were delivered, including 184 sets of twins. Of the 16,058 mothers delivered, 10,016 attended the Cook County

*Presented at a meeting of the Chicago Gynecological Society, December 17, 1937.

Hospital prenatal clinic, and 6,042 mothers were referred from other sources. There were 798 stillbirths and neonatal deaths, a gross mortality rate of 4.9 per cent. This figure includes all infant deaths occurring in gestations of five months or over. In compiling the corrected infant mortality all infants weighing less than 1,500 gm. were considered previable and were deducted. Also, cases in which syphilis and congenital malformations were the sole cause of death were deducted. All other cases were included in the corrected infant mortality, if the fetal heart tones were heard at least once after admission, and if the birth weight was over 1,500 gm. Thus, 509 cases were excluded, leaving a total of 289 deaths, or a corrected infant mortality rate of 1.78 per cent. Of the 509 cases not included, 285 weighed under 1,500 gm. at birth and 224 weighed over 1,500 gm. Two hundred and eighty-four were dead on admission to the Hospital, 50 died of congenital anomalies, 63 died of syphilis, and 102 infants were alive at birth, but died early in the neonatal period because of prematurity (under 1,500 gm.).

In the entire series of 16,242 births, 14,861 were spontaneous, inclusive of 604 breech deliveries which were assisted manually after spontaneous delivery to the umbilicus; 1,381 deliveries were operative, inclusive of 196 bag insertions, a total operative incidence of 8.6 per cent. Among the 14,861 spontaneous deliveries, there were 602 infant deaths, a gross mortality rate of 4 per cent, whereas among the 1,381 operative cases, 196 infants died, a gross infant operative mortality rate of 14 per cent.

Table I represents the results in 634 breech presentations.

TABLE I. BREECH PRESENTATIONS

DELIVERIES		TOTAL DEATHS	GROSS MORTALITY RATE	CORRECTED MORTALITY	CORRECTED MORTALITY RATE
Spontaneous breech	604	47	7.8%	23	3.8%
Breech extraction	30	6	20.0%	5	16.0%
Total breech deliveries	634	53	8.3%	28	4.4%

The 604 cases classed as spontaneous breech deliveries include all cases in which the breech was allowed to deliver spontaneously to the umbilicus and assistance rendered only when necessary; whereas those cases listed as breech extractions refer to cases in which interference was instituted before the umbilicus was visible for a definite reason, usually because of fetal distress. Of the 24 cases excluded, 11 were dead upon admission, 10 weighed under 1,500 gm. at birth and 4 died as a result of congenital anomalies. The advantage of conservative management of breech presentations is indicated in Table I.

An analysis of Table II reveals a gross infant mortality rate in cesarean sections of 15.2 per cent and a corrected infant mortality rate of 8.3 per cent. This high cesarean section infant mortality necessitates further investigation and is classified in Table III as to indication for abdominal delivery.

In this series of 44 infant deaths that were delivered by cesarean section, 15 infants were dead on admission to the hospital. The operation was performed in 10 of these patients for ablatio placentae, in 2 cases for placenta previa totalis in primipara and in 3 for ruptured uteri. Of the remaining 29 cases, three infants weighed under 1,000 gm., the indications for cesarean section being impending eclampsia, 2 cases and ablatio placentae, 1 case. Four infants weighed between

1,000 and 1,500 gm., the indications in this group being impending eclampsia, 3 cases; and tuberculosis for purpose of sterilization, 1 case. Ten infants weighed over 1,500 gm. but less than 2,500 gm. The indications for abdominal delivery in these cases follow: placenta previa, 4 cases; impending eclampsia, 5 cases; and previous cesarean section, 1 case. The remaining 12 infants weighed over 2,500 gm. and were delivered by cesarean section because of disproportion in 4 cases, toxemia in 1 case, placenta previa centralis in 1 case, abruptio placentae in 4 cases, previous cesarean section in 2 cases, and tuberculosis for purpose of sterilization in 1 case. Three infants in this latter group died of congenital anomalies, 1 death was due to syphilis, 4 infants died in the neonatal period from intracranial hemorrhage, two infants died of bronchopneumonia during the second week of life and one died of massive liver hemorrhage. To recapitulate, it will be noted that among the 29 infants alive on admission to the hospital, 7 were previable (under 1,500 gm.), 10 were

TABLE II. GROSS AND CORRECTED INFANT OPERATIVE MORTALITY

OPERATIVE PROCEDURE	NO.	INFANT DEATHS	GROSS INFANT MORTALITY	CORRECTED DEATHS	CORRECTED INFANT MORTALITY
Low forceps	605	31	5.1%	29	4.78%
Midforceps	96	14	14.5%	13	13.5 %
Cesarean section	288	44	15.2%	24	8.3 %
Breech extraction	30	6	20.0%	5	16.5 %
Version and extraction	108	25	23.1%	12	11.6 %
Dührssen's incision	17	3	17.6%	3	17.6 %
Braxton-Hicks version	25	25	100.0%	9	36.0 %

TABLE III. CESAREAN SECTION INFANT MORTALITY

INDICATION	TIMES PERFORMED	GROSS INFANT MORTALITY	CORRECTED INFANT MORTALITY	CORRECTED INFANT MORTALITY RATE
Disproportion	86	4	2	2.3%
Ablatio placentae	24	16	6	25.0%
Placenta previa	41	7	5	12.2%
Toxemia	62	10	5	8.0%
Previous cesarean sections	28	2	2	7.1%
Ruptured uterus	7	3	3	42.4%
Nonobstetric indications	40	2	1	2.1%
Total	288	44	24	8.3%

premature (under 2,500 gm.) and of the 12 remaining mature infants, the operative procedure selected played no part in the death of the infant. As would be expected, the largest number of previable and premature infants delivered by cesarean section occurred in the toxemic group. The lowest mortality (Table III) occurred in those cases where disproportion was the indication for cesarean section. Two of these infants died as a result of congenital anomalies, one hydrocephalus, 1 congenital atresia of the esophagus, 1 infant could not be resuscitated, and 1 infant died on the eighth day of birth of bronchopneumonia.

The Dührssen incision operation was performed 17 times. In 8 instances the presenting part was at the midplane of the pelvis, while in the remainder, the station was at a lower level. Three of these babies died, 2 following difficult mid-forceps operations and the third was delivered by craniotomy following failed forceps.

Transverse presentations were encountered 23 times, an incidence of 0.14 per cent. Fifteen were delivered by version and extraction, 6 of these following bag insertions. Seven of these babies died. Two live babies were delivered by cesarean

section, but in 6 cases delivery was accomplished by decapitation, 4 of which were admitted to the hospital as neglected transverse presentations.

The Voorhees' bag was inserted 196 times, the indications follow:

Induction of labor for toxemia	126
Application of bag for cervical dystocia	19
Placenta previa	28
Transverse presentation	9
Ablatio placentae	9
Prolapsed cord	8

There were 40 infant deaths following the use of the bag. Twelve of these deaths occurred following the induction of labor for toxemia and 16 deaths occurred in cases of placenta previa in which bag insertion was the treatment of choice. This operative procedure was successful in preventing the deaths of the infants in 3 cases of prolapsed cord but failed in 5 other cases. In 12 of the 40 infant deaths, death was due to prolapsed cords following the expulsion of the bag with incomplete dilatation of the cervix. When the use of the bag is indicated because of important maternal complications, the danger to the infant may be regarded as a matter of secondary importance.

Table IV presents the infant mortality as to causation not attributable directly to obstetric operative procedure, and comparing these contributing factors with weight and time of death of the baby.

TABLE IV. TOTAL INFANT MORTALITY (TIME AND CAUSES OF DEATH)

WEIGHT GM.	TIME OF DEATH				CONTRIBUTING MATERNAL CAUSES					
	ANTEPARTUM	INTRAPARTUM	NEONATAL	TOTAL	TOXEMIA	ABLATIO PLACENTAE	PLACENTA PREVIA	SYPHILIS	DIABETES	INTRAPARTUM SEPSIS
Under 1,000	54	6	80	140	11	1	5	7	1	0
1,000-1,500	55	6	84	145	14	2	4	19	0	1
1,500-2,500	78	42	60	180	39	14	14	20	0	6
2,500 - -	104	104	125	333	31	20	21	17	1	14
Total	291	158	349	798	95	37	44	63	2	21

Miscellaneous Causes

WEIGHT GM.	PRE- MATURITY	PROLAPSED CORD	LIVER HEM- ORRHAGE	CONGENITAL ANOMALIES	UNKNOWN
Under 1,000	78	2	0	4	22
1,000-1,500	83	1	1	8	18
1,500-2,500	60	5	2	13	24
2,500 - -	0	11	3	23	50
Total	221	19	6	48	114

There were 95 deaths in which maternal toxemia (eclampsia, pre-eclampsia, and nephritic toxemia) was either the sole or a very important contributing factor to the death of the infant. Twenty-five of these infants were previable or weighed under 1,500 gm., and 18 of these were dead on admission. Of this latter group of 18 infants dead on admission, 9 were delivered following the spontaneous onset of labor, 3 were delivered following a medical induction, 3 following bag inductions, and 3 by means of cesarean section. Of the remaining 7 intrapartum and neonatal deaths, 2 were delivered by cesarean section, 2 delivered after spontaneous onset of labor, 2 delivered after medical inductions, and 1 delivered after a bag induction.

Seventy infants in the toxemia group weighed over 1,500 gm., and of these, 37 were dead upon admission, 11 died during labor, and 22 died during the first two weeks of life.

In the 22 neonatal deaths, autopsies were performed upon 15 infants, revealing 9 deaths due to intracranial hemorrhage. In the total series of 95 cases of infant

deaths, 59 were excluded, leaving 36 deaths as a corrected infant mortality. Of these, 7 infants might have been saved had the choice of delivery been the abdominal route rather than through the natural passages. Nine infants in this group died before the onset of labor while under observation in the ward. These unfortunate deaths occurred following an attempt to prolong the pregnancy before inducing labor, so as to increase the infants' chances for survival. This experience is worthy of consideration in managing cases of toxemia where with the questionable viability of the baby the induction of labor is delayed.

During the period reviewed, ablatio placentae occurred 63 times with 37 infant deaths, a gross mortality rate of 58 per cent (Table IV). Among these, 3 were nonviable and 34 were viable, but of this latter group 22 were dead on admission to the hospital. The corrected infant mortality was 12 deaths or 20 per cent. Twenty-six babies survived this accident, 8 being delivered by cesarean section, 7 by the low forceps operation, 1 by version and extraction following bag insertion, and 9 delivered spontaneously, 1 after bag insertion. In the 7 patients delivered by the forceps operation, evidence of fetal distress with conditions favorable for immediate delivery indicated the operation. The possibility of honest error in making the diagnosis of premature separation of the normally implanted placenta may, at least in part, account for the comparatively low infant mortality. The method of delivery among the 37 infants that failed to survive this accident follows: Spontaneous delivery, 16; classical cesarean section, 2; low cervical cesarean section, 3; Porro cesarean section, 11; low forceps, 3; version and extraction after bag insertion, 3; and spontaneous delivery after bag insertion, 1.

The deaths of 2 of the 12 viable infants were predictable and, had cesarean section been selected for delivery, the lives of these infants might have been saved.

During the four-year period reviewed, there were 127 cases of placenta previa with 44 infant deaths, a gross mortality rate of 34.6 per cent. Twenty-six of these infants were alive and viable upon admission to the hospital, leaving a corrected placenta previa infant mortality rate of 20 per cent. Table V represents the methods of delivery in all cases of placenta previa.

TABLE V. PLACENTA PREVIA MANAGEMENT AND FETAL RESULTS

MANAGEMENT	TOTAL	LIVE BABIES	VIABLE INFANTS DIED	NONVIABLE INFANTS DIED
Abdominal section	41	34	5	2
Spontaneous delivery after bag induction	22	10	10	2
Version and extraction after bag induction	2	2	0	0
Rupture of bag of waters	22	22	0	0
No therapy required	15	15	0	0
Braxton Hicks version	21	0	7	14
Braxton Hicks after bag in- duction	4	0	4	0
Total	127	83	26	18

The 5 viable infants which died and were delivered by cesarean section succumbed during the neonatal period. Two died of bronchopneumonia, 2 of intracranial hemorrhage, and in 1 case the cause of death was undetermined. In 9 cases in which viable infants were lost, conditions were favorable for cesarean section and if performed might have salvaged some of these babies. In the remainder of these cases where viable babies were lost, the patients were bleeding profusely and were in such poor condition upon admission that cesarean section was contraindicated.

There were 21 infant deaths due to sepsis, the fetus succumbing either in the course of the maternal sepsis, or the sepsis resulted in a premature labor, the infants dying shortly after birth. In 14 of these, lobar pneumonia was the cause of the maternal sepsis; in 5, severe pyelitis; in 1, ascending cholangitis; and in 1 other case, bacterial endocarditis.

In the entire series, the mothers of 18 babies that were lost had been referred to the hospital after attempts had been made in the home to effect delivery. Of these, 5 might have been saved by abdominal delivery had not previous procedures made cesarean section too hazardous a procedure for the mother. Nine babies in this group died before delivery or shortly after delivery.

PROLONGED LABOR

There were 26 infant deaths occurring in cases of prolonged labor varying in duration between thirty-eight and one hundred and three hours. In 14 of these cases, the dystocia was definitely functional without evidence of disproportion. That the labors would be prolonged and difficult was recognizable after the first sixteen to twenty hours of labor. The so-called conservative attitude in the management of these cases seemed justified in view of the fact that the dystocia could be attributed solely to inefficient uterine contractions. Since accoucheurs have frequently observed these malfunctioning uteri suddenly adjust themselves after hours of irregular, inefficient contractions and result in a quick and happy termination of labor, we feel that management, conservative versus radical, must be dependent upon the judgment of the individual attendant. Of the 14 cases of inertia, 5 patients delivered spontaneously, 5 by the low forceps operation, 1 by a midforceps operation, 1 by a version and extraction, 1 by breech extraction, and 1 breech was allowed to deliver spontaneously. Had a timely cesarean section been performed in these cases, the results for the baby would have been different.

There were 12 infant deaths occurring in cases of prolonged labor in which disproportion of varying degrees was associated with the dystocia. In 5 cases, the disproportion was not recognized early enough in labor to justify safe abdominal delivery. Three of these patients were delivered by craniotomy after the baby had succumbed, 1 was delivered by a midforceps operation, and the fifth patient delivered spontaneously, the fetal head being markedly molded. In these 5 cases, had the disproportion been recognized, the "modus operandi" certainly would have been obvious. The remaining 7 infant deaths associated with prolonged labors fall in that ever disturbing group of cases of borderline disproportion with uterine dysfunction, and timely cesarean section could have been performed without undue criticism. Of these cases, 2 patients delivered spontaneously, 2 by low forceps, and 2 by the midforceps operation. The "impression method" is used as a routine in the Cook County Hospital to diagnose cephalopelvic disproportion. The failure of the method in these 12 cases was in a great part due to the fact that the amount of molding of the fetal head was not properly evaluated.

In reviewing these cases of prolonged labor, we find that in 26 cases error was made either in failing to recognize the cause of the dystocia or, if recognized early enough, in failing to institute the proper method of delivery.

DISCUSSION

Conflict has been noted in the literature as to the method of reporting infant mortality. It is generally accepted that only infants weighing less than 1,500 gm. and measuring less than 35 cm., head to heel, should be excluded from the corrected infant mortality (Stander¹). On this basis alone the infant mortality at the Cook County Hospital during the period included in this survey would be 513 infant deaths or 3.15 per cent. However, in compiling a corrected infant mortality rate exclusion of only infants below the above weight and length specifications would not present the true picture if a corrected infant mortality rate is to represent the result of obstetric procedure. Deaths which occur in utero before the patients present themselves to the hospital should be excluded from a corrected infant mortality, for regardless of the obstetric procedure, the outcome for the infant is obvious. Similarly,

should neonatal deaths due to congenital anomalies or syphilis be included? It is our opinion that the inclusion of these deaths in a corrected infant mortality is not a true picture of obstetric procedure, and therefore should not be included in a corrected infant mortality. The corrected mortality rate after deducting the deaths of infants under 1,500 gm. and under 35 cm., those dead on admission to the obstetric service, and those deaths due to congenital anomalies and syphilis is 289 or 1.78 per cent for the Cook County Hospital in Chicago.

A study of all cases of prolonged labor is impossible because of inadequate record facilities. As to the question of the more frequent performance of cesarean section, the outcome for the infant might possibly have been different had the operations been performed 9 times for placenta previa, 11 times for uterine dysfunction without disproportion, 11 times for borderline disproportion with uterine dysfunction, and in 7 cases for toxemia. Strangely enough the incidence of cesarean section in our series was 288 or 1.78 per cent. Had cesarean section been performed in 26 cases where the results might have been foreseen, the incidence of cesarean section would then have been 1.93 per cent. Some hospitals have reported cesarean section incidence as high as 14 per cent.

Stander² in quoting Plass, states that about 25,000 cesarean sections are done each year in this country and that probably 75 per cent of these are unnecessary. In the Woman's Clinic of New York City² in a year's period, among 5,456 deliveries, there were 153 cesarean sections, an incidence of 2.8 per cent, with 11 infant deaths. In a ten-year study at the Boston City Hospital,³ among 22,880 deliveries, there were 703 abdominal sections, an incidence of 3.07 per cent. The infant cesarean section mortality was not given. In the Touro Infirmary Obstetric Service⁴ in 1935, in 752 deliveries, 493 of which were private and 259 charity cases, there were 52 cesarean sections, an incidence of 6.5 per cent. In the Margaret Hague Maternity Hospital⁵ in Jersey City, in 8,852 cases, there were 117 cesarean sections, an incidence of 2 per cent with 21 fetal deaths or 11.8 per cent. The corrected cesarean infant mortality in this group was 5.6 per cent. Kushner⁶ reports a cesarean section incidence of 3.4 per cent at the Bronx Hospital in 3,060 deliveries. It is interesting to note that in this same institution which accepts both private and charity patients, the incidence among the ward patients was only 1.9 per cent. There were 11 infant deaths, a mortality of 11 per cent. At the Chicago Lying-in Hospital, E. F. Daily⁷ reports an incidence of 2.86 per cent in a total series including 8,871 hospital patients and 8,622 deliveries in the home service. The incidence among 8,871 hospital cases was 5.6 per cent. In this entire series there were 31 infant deaths, a gross mortality of 5.2 per cent.

J. R. McCord⁸ reports that at the Grady Memorial Hospital, in 1,721 deliveries among colored patients, there were only three cesarean sections, an incidence of 0.18 per cent, the lowest incidence we were able to find. It is especially commendable that the gross infant mortality in this series was 1.8 per cent, the corrected 1.2 per cent.

At the Rotunda Hospital⁹ from November, 1934, to October, 1935, in 2,777 deliveries there were 29 cesarean sections, an incidence of 1.05 per cent and at the Coombes Lying-in Hospital¹⁰ in 1,188 deliveries there were 37 cesarean sections, an incidence of 3.1 per cent with six stillbirths and neonatal deaths, an infant cesarean section mortality of 16.2 per cent.

It is interesting to note that in a three-year period in the entire state of Iowa¹¹ among 91,738 births, the cesarean section incidence was 1.0 per cent.

Reviewing these statistics, it is found that the general infant mortality rate in cesarean section varies from 2 per cent to 16 per cent. Most of

these deaths are due to prematurity when occurring in the neonatal period. Others occur in cases where a dead infant may be expected as in ablatio placentae and placenta previa centralis, where the operation is performed in the interest of the mother. It is in cases of dystocia, such as the 26 cases in this series, where the infant has reached maturity that the more frequent performance of early cesarean section would undoubtedly diminish the infant mortality, without unduly increasing the incidence of cesarean section.

REFERENCES

- (1) *Stander, H. J.*: AM. J. OBST. & GYNEC. 28: 421, 1934. (2) *Idem*: Ibid. 29: 559, 1935. (3) *Duncan, J. C., and Doyle, J. B.*: New England J. Med. 216: 1, 1937. (4) *Levy, W. E., and Meyer, H.*: New Orleans M. & S. J. 89: 132, 1936. (5) *Waters, E. G., and Leavitt, B.*: AM. J. OBST. & GYNEC. 29: 535, 1935. (6) *Kushner, I. I.*: Ibid. 32: 874, 1936. (7) *Daily, E. F.*: Ibid. 30: 204, 1935. (8) *McCord, J. R.*: South M. J. 28: 53, 1935. (9) *Davidson, A. H. et al.*: Irish J. M. Sc. p. 337, Aug., 1936. (10) *Healy, T. M., Tighe, H. V., and Finegan, J. J.*: Irish J. M. Sc. p. 428, Aug. 19, 1936. (11) *Plass, E. D.*: J. Iowa M. Soc. 25: 586, 1935.

700 NORTH MICHIGAN AVENUE
185 NORTH WABASH AVENUE

DISCUSSION

DR. FRED L. ADAIR.—It is difficult to discuss in a brief time a paper which contains such a mass of statistics. Statistics are, of course, definitely helpful in evaluating various procedures and in making comparisons. It seems important, therefore, in connection with any study of statistics to reach some more or less arbitrary standard which can be used not by one but by many. Hillis and Benensohn have pointed out the lack of uniform standards for such a comparative statistical analysis.

At the Chicago Lying-in Hospital we consider as abortions all cases of less than twenty-two weeks' gestation, which is approximately five months. The law says that all cases over five months must be reported as births. The length of the fetus, 28 cm., and the weight, 400 gm., are also used as standard. One encounters certain difficulties in applying these three criteria, but if the fetus complies with any two of them, it should be placed in the abortion group. For example, if a fetus is born which is less than 28 cm. in length and less than 400 gm. in weight, but beyond twenty-two weeks, it would still be in the abortion group. Or, if the gestation period was twenty-two weeks or less and the fetus longer than 28 cm., we would still consider it an abortion.

The next group to consider is the previable group, stopping at 1,000 gm. as the maximum weight, 400 gm. the minimum; length, 28 to 35 cm.; and period of gestation, from twenty-two to twenty-eight weeks. One thousand grams have been placed as the upper margin of previability, because we find that relatively few infants survive who are under 1,000 gm. in weight. In a study of six hospitals, Dr. Dunham found that 5 of the 6 showed no survivals under 1,000 gm. One institution had 5 per cent survivals. We have had about 1.2 per cent survivals at the Lying-in Hospital, but only a very few of these babies do survive, so the term previability seems applicable to the group under 1,000 gm.

The term premature-viable is applied to fetuses weighing under 2,500 gm. and over 1,000 gm., with a length of 35 to 47 cm., and a gestation age from twenty-eight to thirty-seven weeks.

The mature fetus weighs from 2,500 to 5,000 gm., is from 47 to 54 cm. in length, and from 38 to 43 calendar weeks' gestation.

Then we have a group of excessive size fetuses which presents a problem. They can be called postmature or oversized and the following criteria for classifying them have been set: more than 4,500 gm. in weight; over 54 cm. in length; and more than forty-three weeks' gestation age.

The following terms have also been adopted: antenatal death, when death occurs before the onset of labor; intranatal death, when death occurs during labor; postnatal death, when the fetus shows signs of life at birth but in whom no respiration is established; and then the final or neonatal group in which the baby is born alive but dies before leaving the hospital, usually within a two weeks' period.

That represents our grouping. There is insufficient time to discuss all the factors that have been brought out by Hillis and Benensohn in their very complete presentation. It seems that, in correcting statistics, one has to distinguish between the mortality which is attributed to the institution and the mortality which is assigned to some procedure or condition associated with the death. The statistics on institutional mortality must remain as institutional mortality; they really cannot be corrected. Deaths that occur in the institution are chargeable to the institution, although not necessarily in the sense that the institution is responsible. When, however, one attempts to evaluate a given procedure from a scientific point of view, then an attempt should be made to evaluate that procedure as far as the results are concerned in mortality and morbidity. Naturally one cannot assign the death of a fetus to an operation when the fetus was already dead before the operation was begun. Certain corrections then would be justifiable in evaluating statistics of causes of death whereas one would not be justified in correcting total institutional figures.

I want to say a few words about cesarean section. It is done for the benefit of both the mother and the fetus. Ordinarily it is considered a safe procedure as far as the baby is concerned. I think these statistics emphasize the fact that there is a definite fetal mortality associated with cesarean section, and our findings at the Chicago Lying-in Hospital furnish confirmation of this thought. From May 1, 1931, to October, 1936, we had 838 sections, which was 5.8 per cent of our total deliveries for that period. There were 49 infant and fetal deaths, a total mortality of 5.8 per cent. The stillbirth rate was 1.2 per cent; the neonatal mortality rate, 4.6 per cent. If we consider the uncorrected mortality for all the cases in the hospital, the neonatal mortality was 1.83 per cent compared with the 4.6 per cent associated with cesarean section. Our stillbirths were somewhat higher in the non-cesarean than in the cesarean group. In other words, we did not do cesarean section when the baby was already dead or in a precarious condition.

It was interesting to study why a larger percentage of cesarean babies should die neonatally—why the neonatal mortality in our cesarean section group was 4.6 per cent, whereas the uncorrected neonatal mortality for all cases in the hospital was less than 2 per cent. Of the 49 fetal deaths (4.6 per cent), 31 were neonatal and 18 were stillbirths. The neonatal were associated with abruptio placentae in 8, placenta previa in 2, malformation in 4, eclampsia in one, and with premature birth and undetermined cause in 16. Of these 31 neonatal deaths, 19 infants weighed less than 2,500 gm. Of the 18 stillbirths, 15 were associated with abruptio placentae, 2 with placenta previa, and one with eclampsia.

In a subsequent series of 338 sections we have had 18 infant and fetal deaths—14 were neonatal and 4 were stillbirths. Of these 18 deaths, 4 (of which 3 were stillbirths) were associated with placenta previa, 4 with abruptio placentae, 3 with heart disease, 3 with previous section, one with transverse presentation, one with prolonged labor without progress, one with epilepsy, and one with Porro section.

One must recognize that about one out of 20 babies is lost when cesarean section is done. It behooves us therefore to select cases very carefully when there is not a strict maternal indication for this operation. Every effort should be made to secure 100 per cent fetal survival in association with cesarean section.

DR. WILLIAM C. DANFORTH.—I would like to offer for comparison with the report of Dr. Hillis some figures from our service which differs from that of the County Hospital in that a considerable percentage of our patients are private cases. Eighty per cent of the work in the maternity is done by the departmental staff, all of whom also belong to the Department of Obstetrics and Gynecology of Northwestern University Medical School. There is also a selected group of practitioners. Uniformity of technic is therefore not difficult to maintain.

In the past nine years there were 7,461 deliveries. The infants numbered 7,536. The gross fetal mortality was 3.77 per cent. Subtracting the number of infants which were premature, which were born with some anomaly incompatible with continued life or which were dead when labor began as evidenced by absent heart tones, we have a corrected mortality of 1.15 per cent.

Our figures vary materially from those given by Hillis in some particulars. The number of spontaneous deliveries is far less and the incidence of operative delivery is much higher. An analysis of our work, however, indicates that the great majority of our operative deliveries are low forceps. In the entire series of cases there were only three high forceps deliveries and but 217 midforceps. Our outlet forceps are greatly increased in number by the frequent use of analgesic agents. As most of the work is done by trained men we have not tried to limit the number of outlet forceps deliveries. A study of infant mortality and its relation to various procedures made two years ago showed that infant loss of life in spontaneous delivery and that with outlet forceps were nearly identical, the mortality with outlet forceps being 0.1 per cent less than when the infants were allowed to deliver spontaneously. Outlet forceps in trained hands is not a radical procedure. A clear indication must exist for the use of midforceps and high forceps should be an exceedingly rare operation.

In the County Hospital series version and extraction occurred 108 times in 16,242. In our series 123 versions were done in 7,461 labors, the incidence being 1.63 per cent. The Cook County series lists 634 breech deliveries. I agree with the recommendation that a labor with a breech position should be allowed to proceed normally until the breech is delivered, interference beginning only after this. The wisdom of this is shown in the figures quoted, the mortality in those cases managed conservatively being far less than when extraction was needed.

Recently Galloway, in our service, collected figures upon a series of 285 breech cases occurring in 8,531 labors. Of these patients 188 were delivered at term, the mortality in this group being 5.85 per cent. A very marked difference was found between the mortality rate in the group at term and the premature infants. The greatest mortality was in the group under seven months gestation, in which the mortality was 96 per cent. In the group of infants weighing five pounds or more the mortality was 6.5 per cent.

DR. HILLIS (closing).—The inclusion in the mortality lists of babies weighing between 1,000 and 1,500 gm. raises the death rate considerably. From a mechanical standpoint a baby that weighs less than $3\frac{1}{4}$ pounds is not a very important item in the delivery. Such babies usually deliver spontaneously, forceps are not used and the version, with conditions present, is a simple thing. The death of such babies is entirely beyond the control of the attendant.

The value of prenatal care at Cook County Hospital agrees with all other large series and indicates that the death rate in the babies is much lower when the patient has been under observation during her pregnancy. Most of the benefits come from the early recognition of syphilis and the toxemias of pregnancy. We believe, at the Cook County Hospital, that impression of the head is a valuable aid in the diagnosis of disproportion between the head and the pelvis.

With respect to the forceps operation, this series indicates that 4.3 cases in every 100 require some kind of forceps delivery. The mortality in these indicated forceps operations was 4.8 per cent. To these deaths should be added 23 cases in which the baby died where low forceps should have been done in the second stage.

The infant mortality in breech labor is generally said to be 8 to 15 per cent. It is well known that unnecessary interference in a breech labor contributes largely to infant death. It requires considerable poise to allow a breech case to deliver spontaneously as far as the navel, especially if one does not constantly know that the baby is in good condition. At the Cook County Hospital the head stethoscope is worn in every labor during the second stage and the breech cases are allowed to deliver spontaneously as far as the navel. Manual aid is done only when necessary and breech extraction is never done except for a definite reason.

THE ACTIVATION OF UTERINE MUSCLE BY ESTRIN AND ITS RELATION TO UTERINE GROWTH

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DURING proestrus and estrus, the myometrium exhibits a characteristic pattern of motility. Each intermittent contraction of the uterus normally arises as a continuation of a tubal contraction, every fourth or fifth one of which finds the uterus relaxed and ready to contract again.^{25, 31} This wave of myometrial contraction sweeps slowly over the length of the uterus and subsides as it reaches the cervix. Not only does the whole intact uterus show this dominance of the upper portion over the lower one but parts of the uterus, excised as well as in situ, show a similar gradient of activity independently of the tubes.^{4, 7, 8, 16, 17, 21, 32 et al.} The effect is perhaps most strikingly shown when the contraction frequencies of the upper and lower ends of a uterine horn are investigated separately, for it is found that the tubal segment has a higher frequency of contraction than does the cervical end studied under similar conditions.^{4, 12, 14}

Such a gradient of activity is dependent upon the hormone, estrin, which is the hormone responsible for the other manifestations of estrus.²⁶⁻²⁸ Careful consideration of the data at hand shows that the manner in which estrin exerts its effect upon the myometrium is ascribable to the action which this hormone has upon the cells of this tissue and not to any known effect which it may have upon the innervation, extrinsic or intrinsic.^{16, 27} The action is, therefore, essentially a metabolic one.

Ample evidence exists which shows that the uterus has a higher rate of oxygen consumption at the time of estrus than it does at any other time in the nongravid state,^{3, 10, 18-20} and this, like myometrial activity, has been shown to be due to the action of estrin.^{3, 10, 18, 20} Up to the present time, however, no evidence has been adduced which shows whether the increased oxygen utilization of the uterus is attributable to the marked activity which the myometrium undergoes at this time, as suggested by King,¹⁹ or whether the uterus is active because there is an initial increase in the rate of oxygen consumption prior to the onset of motility. Experiments bearing upon this point have recently been performed.

THE METABOLIC STIMULUS IN RELATION TO ONSET OF MOTILITY

When estrin is injected into suitable ovariectomized animals, a rise in the rate of oxygen consumption takes place within a few hours.

*Fellow, John Simon Guggenheim Memorial Foundation. The writer expresses his appreciation to Professor George W. Corner for advice and hospitality extended to him during tenure of the fellowship.

Thus, in gonadectomized, immature rabbits the oxygen consumption increases 20 per cent in five hours (after a single subcutaneous injection of 500 international units of estradiol); by the tenth hour, it increases 37 per cent and by the twenty-fourth hour, the rate of oxygen consumption is 60 per cent greater than before the administration of estrin (see Fig. 1, Curve B). Thus the effect is approximately two-thirds complete by the tenth hour after the injection of estrin.²⁰

This fact is significant when it is recalled that under the most favorable circumstances of estrin administration the myometrium shows no appreciable motility for about ten hours,^{5, 25-27, 29} and from this time on, until the twenty-fourth hour or thereabout, the activity of the myometrium increases progressively to maximal forcefulness and rhythmicity (see Fig. 1, Curve C). Pertinent also is the observation that addition of estrin to a bath containing inactive uterine tissue fails to render the myometrium active; in order for excised tissue

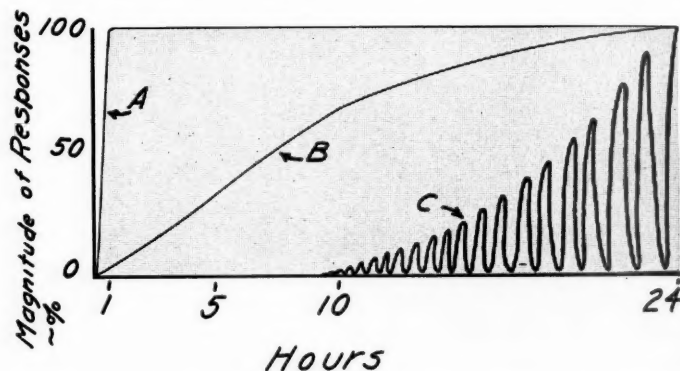


Fig. 1.—Diagram showing the relation of certain effects of estrin upon the uterus after administration to a rabbit. A, initial hyperemia of small vessels in the uterus (endometrial and myometrial); B, oxygen consumption of uterine tissue; C, the development of uterine contractions in vivo. Ordinate, the magnitude of the several responses in terms of percentage of the maximal response; abscissa, time in hours after a single subcutaneous injection of estradiol or other estrogenic hormone.

to exhibit estrous motility the hormone must have acted first in vivo.^{5, 15, 22, 24, 28, 29} Clearly, therefore, the onset of the estrous type of motility is preceded by an appreciable elevation of metabolic activity of the uterus which has been achieved only in vivo up to the present time. Hence the onset of this type of motility signifies that a certain phase of the uterine growth response to estrin has been attained. That myometrial activity is not essential for endometrial growth is shown by the fact that transplants of endometrium grow in the anterior chamber of the eye in the absence of myometrial tissue.^{21, 23} For the organ as a whole, however, and for the myometrium alone, perhaps, the intermittent contractions of estrus do play an important role which has been appreciated only in the past few years.

THE ROLE OF INTERMITTENT UTERINE CONTRACTIONS DURING ESTRUS

Prominent among the effects which estrin has upon the uterus is the vascular change which comes about within a few minutes after the injection of the hormone. Within twenty minutes to half an hour, a state of maximal hyperemia exists^{21, 23, 25} which persists as one of the most striking of the phenomena associated with the response of the uterus to estrin (see Fig. 1, Curve A). As a result of this hyperemia enlargement of the capillary bed, increase in the permeability of the vessels, particularly in the endometrium, and accumulation of appreciable quantities of fluid in the stroma of this structure take place.¹³ These effects are well developed before the myometrium is motile and, according to the evidence at hand, they precede any significant rise in the metabolic activity of the uterus.²⁰ This consideration suggests that the increase in vascularity which takes place first is the result of a special, direct mechanism whose chief function is to assure an adequate circulation to an ischemic organ whose blood vessels are small, which has a low level of metabolic activity and which is non-motile. Enlargement of the vascular bed by a local vasodilatation thus provides the tissue with an ample supply of blood. That a vasodilating substance is elaborated locally is shown by the fact that the initial hyperemia takes place in transplanted uterine tissues in which nerves have not been demonstrated,^{21, 23} and since the hyperemia can be temporarily inhibited by the injection of atropine.²⁵ As yet, however, existence of this vasodilating substance has not been directly proved, although the initial vasodilatation has.*

Thus far the relation of uterine activity to the preliminary vascular and metabolic changes has been only a subject of theoretical discussion^{13, 27} and not one of direct investigation. The conclusion has been reached, on the basis of sound physiologic considerations, that the intermittent uterine contractions serve to augment the volume flow of blood through the already dilated vessels of the uterus, owing to the pumping action of the myometrial movements. Such, at least, is the effect of intermittent activity in skeletal muscle and of rhythmic intestinal movements.² Activity of this type has been found to be essential, moreover, for the formation and flow of lymph from a number of structures.¹¹ It is for this reason, no doubt, that only at the time of estrus can the lymphatic vessels of the female genital tract be injected with ease.¹ By inference, therefore, it appears that the plasma fluid which contributes to the edema of the endometrium after administration of estrin tends to be removed by the intermittent uterine contractions of estrus;^{13, 27} failure of such an action would predispose to retention of large quantities of fluid in this tissue. It is clear from these considerations, then, that the uterine contractions which are induced by estrin serve the purpose in the intact animal of assuring an adequate circulation through tissues which are under-

*Experiments done since this was written established that this substance exists and is identical in its reactions with acetyl-choline. An account of these experiments will be published elsewhere.

going marked growth changes coincidently. Because of the fact that the uterine motility of estrus is in reality part of the uterine growth response, as noted above, one may thus say that uterine growth is its own best means of providing an ample blood supply for itself. Nature has made sure, therefore, that that hormonal agent which is the primary metabolic stimulus to the uterus anticipates this action by supplying blood through the agency of a local vasodilatation and subsequently provides an adequate mechanism for the facilitation of the circulation of blood through, and of lymph from, the growing organ at a time when the nutritive requirements are increased. That this mechanism is a beneficial one is shown as a result of experiments on animals.

AUGMENTATION OF UTERINE GROWTH BY AUGMENTATION
OF THE BLOOD SUPPLY

The experiments which show the importance of the local blood supply for uterine growth are not new. They were performed a number of years ago by Buchheim and Zaleski⁶ who studied its relation to endometrial growth, and by Courrier and Bouin⁹ who studied its relation to myometrial growth. The methods and results were similar, only the tissues were different. In one set of experiments⁶ a transplant of endometrial tissue was made to each ear of a rabbit, in the other,⁹ myometrial transplants were made. After the transplants became established, the cervical sympathetic nerve to one ear in each rabbit was sectioned. The composition of the blood flowing to each ear was, of course, identical although the volume flow of blood was much increased in one ear and not in the other. It was found, as a result of these procedures, that the amount of growth on the side with the increased blood supply was far greater than it was on the opposite, control side. Indeed, Buchheim and Zaleski state that the amount of growth observed by them was almost pathologic.

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While it is evident, therefore, that the effect of estrin on uterine tissues is chiefly that of a growth-promoting agent, the other uterine effects brought about by the same hormone play a subsidiary but important role which assures that the main effect will take place in due time. The initial vasodilatation of the small vessels provides an immediate and easy access of blood to the inactive uterine tissues whose metabolic processes are at low ebb. As the hormone raises the metabolic activity of the uterus to a certain level the myometrium becomes rhythmically active, and this motility in turn aids the growth changes which proceed simultaneously through the agency of the improved state of the local circulatory conditions. Thus these several effects which are brought about in the uterus by the administration of estrin are so inter-related that uterine growth is achieved, from the physiologic point of view, in a most efficient manner.

REFERENCES

- (1) *Andersen, D. H.*: Contrib. Embryol., Carnegie Inst. of Washington 19: 135, 1927. (2) *Anrep, G. V.*: Harvey Lectures 30: 146, 1934-35. (3) *Aschheim, S., and Gesenius, H.*: Arch. f. Gynäk. 153: 434, 1933. (4) *Blair, E.*: Anat. Rec. 12: 9, 1922. (5) *Blair-Bell, W., Datnow, M., and Jeffcoate, T. N. A.*: J. Obst. & Gynaec. Brit. Emp. 40: 541, 1933. (6) *Buchheim, W., and Zaleski, W.*: Compt. rend. Soc. de Biol. 104: 896, 1930. (7) *Clark, A. J., Knaus, H., and Parkes, A. S.*: J. Pharmacol. & Exper. Therap. 26: 359, 1926. (8) *Corner, G. W.*: Am. J. Anat. 32: 345, 1923-24. (9) *Courrier, R., and Bouin, R.*: Arch. d. anat. micr. 25: 189, 1929. (10) *David, J. C.*: J. Pharmacol. & Exper. Therap. 43: 1, 1931. (11) *Drinker, C., and Field, M.*: Lymphatics, Lymph and Tissue Fluid, Baltimore, 1933, Williams and Wilkins. (12) *Durrant, E. P., and Rosenfeld, S.*: Am. J. Physiol. 98: 227, 1931. (13) *Fagin, J., and Reynolds, S. R. M.*: Am. J. Physiol. 117: 86, 1936. (14) *Harne, O. G.*: Am. J. Physiol. 99: 227, 1931-32. (15) *Jeffcoate, T. N. A.*: J. Obst. & Gynaec. Brit. Emp. 39: 67, 1932. (16) *Kaminester, S., and Reynolds, S. R. M.*: Am. J. OBST. & GYNEC. 30: 395, 1935. (17) *Keye, J. D.*: Johns Hopkins Hosp. Bull. 34: 60, 1923. (18) *Khayyal, N., and Scott, C. M.*: J. Physiol. 72: 13, 1931. (19) *King, J. L.*: Am. J. Physiol. 99: 631, 1931-32. (20) *MacLeod, J., and Reynolds, S. R. M.*: Am. J. Physiol., 1938. Proc. Soc. Exper. Med. 37: 666, 1938. (21) *Markee, J. E.*: Am. J. Physiol. 100: 374, 1932. (22) *Marrian, G. F., and Newton, W. H.*: J. Physiol. 77: 4, 1932. (23) *Neumann, R.*: Arch. f. Gynäk. 157: 548, 1934. (24) *Newton, W. H.*: J. Physiol. 79: 301, 1933. (25) *Pompen, A. W. M.*: De Invloed van Menformon op der Baarmoeder, Thesis, Amsterdam, 1933. (26) *Reynolds, S. R. M.*: Am. J. Physiol. 97: 706, 1931. (27) *Idem*: Physiol. Rev. 17: 304, 1937. (28) *Robson, J. M.*: J. Physiol. 79: 139, 1933. (29) *Idem*: Recent Advances in Sex and Reproductive Physiology, New York, 1934, P. Blakiston's Son & Co. (30) *Robson, J. M.*: J. Physiol. 85: 145, 1935. (31) *Westman, A.*: Acta obst. Scandinav. 5: suppl. 3, 7, 1926. (32) *Wislocki, G. B., and Guttmacher, A. F.*: Johns Hopkins Hosp. Bull. 35: 246, 1924.

SURGICAL TREATMENT OF DYSMENORRHEA*

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THE many types of treatment, both medical and surgical, which have been proposed for the cure of dysmenorrhea are so numerous that it is evident that no type of treatment is entirely satisfactory. In an attempt to evaluate the results of treatment of dysmenorrhea, the histories of 682 cases were reviewed. These cases included all those in which a diagnosis of dysmenorrhea was made at the Mayo Clinic between Jan. 1, 1931 and Jan. 1, 1934. In 112 cases the dysmenorrhea was not considered of sufficient severity to require medication. In 405 cases medical management alone was instituted. These cases have been the subject of a previous report by Stacy and Shoemaker. Surgical treatment was advised but refused by the patient in 37 cases and 128 patients underwent operations. In the paper by Stacy and Shoemaker the total number of cases in which medical treatment was employed was given as 391, and the number of cases in which surgical treatment was employed was given as 104. In reviewing these figures for the present paper, it was discovered that the 38 cases which were discarded from consideration because lesions in the pelvis were thought to be responsible for the dysmenorrhea included 14 patients who received medical treatment and

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24 patients who underwent surgical treatment but failed to reply to the questionnaire. The total number of patients in whom medical treatment was employed, therefore, should have read 405 and the total number of patients in whom surgical treatment was employed should have read 128. The results of these operations will be the subject of this report. Follow-up letters were sent to all the patients who underwent operation. Thirty-four patients were not heard from; this leaves 94 cases in which the state of health of the patient is known one or more years after operation.

It is somewhat difficult to evaluate the efficacy of any one operation in the relief of dysmenorrhea as one or more surgical procedures frequently were done at the one operation, depending on the pathologic condition which was present. Therefore, the cases have been grouped according to the most important surgical procedure performed.

Resection of the presacral nerve has been the subject of much interest in the surgical control of dysmenorrhea. The pain was considered severe enough to warrant the performance of this operation in 15 cases (Table I). In 7 cases other surgical measures were carried out at the

TABLE I. RESULTS OF OPERATIVE TREATMENT IN CASES OF DYSMENORRHEA

TYPE OF OPERATION		TOTAL NUMBER	RELIEF		
			COMPLETE	PARTIAL	NONE
Resection of pre-sacral nerve	Alone	8	2	3	3
	With resection of endometrial implants	3	2	1	0
	With uterine suspension	3	1	1	1
Uterine suspension	With myomectomy	1	1	0	0
	With resection of ovaries	5	2	2	1
	With removal of endometrial implants	1	0	1	0
	With dilatation and curettage	3	0	2	1
Dilatation and curettage	With myomectomy	3	2	0	1
	Alone	26	5	12	9
	With removal of cervical fibroid	1	1	0	0
	With partial resection of ovaries	2	0	2	0
	With myomectomy	1	0	0	1
Partial resection of ovaries		2	0	1	1
Myomectomy		3	1	1	1
Insertion of a Baldwin tube		4	0	2	2
Miscellaneous	Watkins-Wertheim interposition	1	1	0	0
	Salpingectomy	1	0	1	0
	Exploratory laparotomy and freeing of adhesions	1	0	0	1
	Total, combined with removal of ovaries	14	6	8	0
Hysterectomy	Total, without removal of ovaries	7	2	5	0
	Subtotal, combined with removal of ovaries	4	3	1	0
Total		94	29	43	22

same time; namely, resection of endometriosis in 3 cases, suspension of the uterus in 3 cases, and myomectomy in one case. In 5 cases complete relief of the dysmenorrhea followed the operation, and in another case relief was complete for two months and then the patient had a recurrence of pain which was, however, controlled by the administration of acetylsalicylic acid. Four patients were definitely improved; another patient rated her improvement at 75 per cent. Four of the patients reported no relief at the time they received our letters. This does not necessarily mean that the operation itself was at fault, but points to the use of caution in the selection of patients for resection of the presacral nerve. The mental make-up of the patient must be taken into consideration as well as the physical findings. This is well illustrated by a case in which the patient, who was a young girl, is still suffering a year after her operation. Resection of the presacral nerve was requested, as a last hope, by the family against the advice of both the physician and the surgeon, who realized that the mental attitude of the patient was such that there was no hope for alleviation of the pain.

Retroversion has long been diagnosed as the cause of many symptoms among these patients. In 12 cases in this series a suspension of the uterus was done as the primary surgical procedure. Additional pathologic changes necessitated partial resection of the ovaries in 5 cases. Removal of endometrial implants, dilatation and curettage, or myomectomy was also done in some cases. Four patients reported complete relief of their monthly pain. Two of these had undergone partial resection of the ovaries and two had undergone myomectomy in addition to suspension of the uterus. Five patients obtained partial relief of their pain and only 3 reported that they did not experience any relief as a result of the operation. Two of these patients had undergone the same two types of operation as had the 4 patients who obtained complete relief. The third failure followed a dilatation and curettage in combination with the suspension.

Dilatation and curettage was long considered to be the treatment par excellence in cases of so-called obstructive dysmenorrhea. It is often the operation of choice because there is a coincident sterility, which, if relieved, may cure the menstrual pain. However, in this group of cases there were only three in which sterility also was a factor. Dilatation and curettage was the only surgical procedure employed in 26 cases; in 2 cases it was done in combination with myomectomy, and in one of these cases the myomectomy was performed by the vaginal route in the course of removal of a pedunculated submucous fibroid. In 2 cases it was done in combination with resection of the ovaries. Five patients obtained complete relief, but another patient reported that she had obtained complete relief for one year. Fourteen patients were improved for from three months to two years. Ten reported no benefit at all from the procedure. Myomectomy was performed twice in conjunction with dilatation and curettage. In the case in which it was performed in the course of removal of a pedunculated submucous fibroid protruding through the cervical os, the patient obtained complete relief, but in the

case in which it was performed for the removal of a subserous myoma, the patient did not obtain any relief. Improvement occurred in both of the cases in which partial resection of the ovaries was combined with dilatation and curettage.

Partial resection of the ovaries was the only surgical procedure employed in 2 cases. Improvement occurred in one of these cases, but no improvement was noted in the other case.

Myomectomy was performed alone in 3 cases. Complete relief occurred in one of these cases, partial relief occurred in another case, but no benefit was noted in the third case.

In 4 cases a Baldwin tube was inserted for a short period of time, presumably to provide dilatation of the os. This operation was popular some years ago, but as little success attended the procedure, it has been almost discarded in recent years.

In 3 cases miscellaneous operations gave varying results. Complete relief was experienced after a Watkins-Wertheim interposition operation for prolapse of the uterus. A salpingectomy produced improvement in one case, but an exploratory laparotomy and the freeing of some adhesions failed to influence the dysmenorrhea in another case.

In 37 cases the severity of the dysmenorrhea, combined with the age of the patient and the pathologic findings resulted in the performance of a hysterectomy. A few of these patients were in their early thirties but the majority of them were more than forty years of age. Twelve of the patients who were subjected to this operation did not reply to our letters, so we have definite information in only 25 cases in which this operation was employed. In 11 of these cases the patients have felt completely well since the operation and have not had pain of any kind. In 8 of these 11 cases a total abdominal hysterectomy was performed and some ovarian tissue was preserved in all but two of them. Endometriosis was also present in one of the cases. Subtotal hysterectomy was performed in only 4 cases; in one of these cases the etiology of the pain, which had occurred between the menstrual periods and had been relieved by the onset of the menstrual flow, was pelvic tuberculosis.

In 14 cases the patients reported that they still had pain. In 9 of these cases, ovarian tissue was preserved, the right ovary was preserved in 7 of these cases, both of the ovaries were preserved in 2 cases, and in 5 cases all ovarian tissue was removed. In 6 cases the pain is mild and in 2 cases it is more severe. The patients described it as a soreness or dull aching which may be situated in any part of the abdomen; it occurs only when they are tired, and it is of short duration. Only 2 patients mentioned any periodicity of the pain. One described a steady pain in the center and right side, and said that "the last part of the month is worst." A patient who was subjected to total hysterectomy wrote that she experienced pain in the right lower quadrant of the abdomen at the menstrual period and at other times if she exerted herself or did any work. In both these cases the right ovary had been partially resected to preserve some ovarian function. A tender ovary may be the cause of the

pain. In one case the pain in the lower part of the back had been so severe that she had taken roentgenologic treatments two to three times a year for relief. Her health is poor. In the three remaining cases in this group, the pain is situated in the right upper quadrant of the abdomen. It is difficult to evaluate the symptoms in these cases from the answers to the questionnaire and in many if not all cases it is probable that the present pain is different from the previous dysmenorrhea. In one case at least, the pain would seem to be attributable to the gall-bladder, if one can judge from the patient's description.

SUMMARY

Surgical intervention for the alleviation of dysmenorrhea produced complete relief in 29 cases and was of benefit in an additional 43 cases. In 14 cases in which hysterectomy was performed the patients still complain of some pain which can be attributed to a tender ovary in some of the cases. In 22 cases there was no relief of the dysmenorrhea. The only procedure which produced uniformly poor results was the insertion of the Baldwin tube, but this procedure has subsequently been discarded.

REFERENCE

- (1) Stacy, Leda J., and Shoemaker, Rosemary: *AM. J. OBST. & GYNEC.* 33: 67, 1937.

THE SAFETY AND ADVANTAGES OF OFFICE CURETTAGE*

AN EVALUATION OF THE ENDOMETRIAL FINDINGS IN 305 PATIENTS

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FOURTEEN years ago, Howard A. Kelly,¹ in addressing this Society, advocated office curettage in this manner: "In doing this I suggest a technic for the specialist, which I condemn for the general practitioner lacking special skill and experience. Let it therefore be made plain that I speak only to gynecologists and of curettage for diagnostic purposes. . . I have seen no accidents following this procedure. I have made innumerable examinations of suspectedly healthy uteri, many of carcinoma of the body and intracervical, and occasionally find retained decidual products."

The value of endometrial study in gynecologic patients is now too obvious to require emphasis. Such study is not only informative concerning the presence or absence of malignancy but, inasmuch as pituitary-ovarian function is usually mirrored in the endometrium, study thereof is also helpful in an evaluation of the patient's endocrine status. In respect to the latter, endometrial study is often more useful than both blood and urine hormone determinations. The desirability of recognizing an early adenocarcinoma and the value of detecting a

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hormonal basis for dysfunctional menstrual disorders or sterility are appreciated by all gynecologists. It is then not surprising that endometrial biopsy, performed without anesthesia, has been widely adopted as an office procedure.

Various cannula-like instruments have been devised for biopsy of the endometrium (Klingler and Burch,² Lörinez,³ Novak,⁴ and Randall⁵). In our experience, these instruments are inadequate for diagnostic purposes even in dysfunctional states of the endometrium, inasmuch as one procure at best only 4 strips of tissue which may not be representative of the endometrium as a whole. That the response of different portions of the endometrium varies greatly to hormonal stimulation was shown previously (Bartelmez,⁶ Traut and Kuder,⁷ and Mazer⁸). While one may reasonably contend that the biopsy technic is sufficient in the study of selected endocrinopathies and sterility, it is certainly inadequate in the differential diagnosis between benign and malignant uterine bleeding. For these reasons, we employ diagnostic office curettage, usually without anesthesia, as suggested by Kelly,¹ in preference to the cannula-biopsy technic.

The most important indication for a diagnostic curettage is menometrorrhagia in women at or just beyond the climacterium when malignancy of the uterine fundus is frequently encountered. Many women are either unwilling or financially unable to enter a hospital for this purpose unless the imminent danger of overlooking a carcinoma is broached. Most patients insist on medical treatment for the control of uterine bleeding before consenting to hospitalization. This is the age of carcinomaphobia when one hesitates to dangle the threat of cancer before the average patient, especially, when the incidence of carcinoma in menometrorrhagia encountered in office practice, as illustrated in the present series, is only 3 per cent (5 in 163 cases, Table II). On the other hand, no physician is justified in assuming that abnormal uterine bleeding at any age is benign without recourse to definite diagnostic measures. When the possibility of carcinoma is not brought to the patient's attention, there is more than a likelihood of procrastination and loss of valuable time in detecting the true state of affairs. Illustrative of the tendency of women to neglect abnormal uterine bleeding is the fact that only 88 (52.7 per cent) of the 163 patients curetted for menometrorrhagia submitted even to an office curettage during the first three months of arrhythmic bleeding. By employing office curettage, the gynecologist avoids delay in diagnosis and spares the patient the unpleasant anticipation of hospitalization and the expense of an operating room procedure.

SELECTION OF PATIENTS AND TECHNIC

The use of the fenestrated curette as an office instrument demands the application of an aseptic technic and a modicum of both art and skill, which remove it to the realm of the gynecologist. Obviously, in selecting the patients for office curettage, certain rules of exclusion must be observed. The procedure may be readily undertaken in all married women with aberrations of the menstrual function

or sterility, *unless* the history and preliminary pelvic examination suggest the presence of either an accident of pregnancy or pelvic inflammation. The present series, in which these criteria were rigidly applied, illustrates the relative harmlessness of office curettage. Only 2 (0.65 per cent) of the 305 patients had a temporary reaction in the form of pelvic pain and slight rise in temperature. Perforation of the uterus in 1 of the 2 patients and a mild infection in the other necessitated rest in bed for a week.

The preparation of the patient is performed as inostensibly as is possible in order to avoid the annoying emotional reaction which, in the average woman, follows the warning that a technical procedure is to be undertaken. The instruments required, previously sterilized, are kept from the patient's field of vision. She remains in the usual lithotomy position following the bimanual examination which always precedes the curettage. The vulva and vagina are cleansed with tincture of green soap and water. The portio, exposed by a bivalve speculum, is painted with 3 per cent tincture of iodine and grasped by a bullet forceps. The bivalve speculum is replaced by a weighted one. The cervical canal is then iodized and the direction and depth of the uterine cavity verified by the passage of a uterine sound. In multiparous women, the smallest (No. 1) Sims' sharp curette may then be passed without difficulty. However, in some nulliparous women, the cervical canal is narrow and requires preliminary dilatation. In such instances, the smallest metal dilator, moistened by a sterile water-soluble lubricant, is passed beyond the internal os. Following this, the curette readily enters the uterine cavity, sedulous care being observed to avoid injury to the neighborhood of the internal os. The interior of the uterus is assiduously investigated and curetted in a routine manner. At the conclusion of the procedure, the patient is permitted to rest on the table for from ten to fifteen minutes and instructed to remain at rest at home until the following morning.

The endometrial tissue, escaping easily from the cervical canal, is collected and immediately placed in 4 per cent solution of formalin for fixation. All fragments of tissue are subsequently hardened in alcohol, sectioned in paraffin, and stained by a routine hemotoxylin-eosin technic. By this procedure, a microscopic diagnosis of the endometrium is possible within seventy-two hours.

When this procedure is gently performed and when the mobilization of the cervix is preceded by a soothing word of warning, the patient experiences no pain up to the point of actual curettage. Anesthesia is generally not required but, if the patient is unusually apprehensive, a brief inhalation anesthesia may be employed at this time. Approximately 10 per cent of our patients were rapidly and safely anesthetized for momentary periods by ethyl chloride inhalation. Although this anesthetic has proved eminently satisfactory in our hands, we are, nevertheless, cognizant of its inherent dangers and recently have employed in these instances nitrous oxide and oxygen from a portable inhalation apparatus.

ANALYSIS OF 305 OFFICE CURETTEMENTS

The present report comprises a series of 305 consecutive office curettements performed during the period between Oct. 1, 1934 and Oct. 1, 1937. The youngest patient was 19 years of age and the oldest 64. Of the 305 women, 160 had borne 1 or more children and the remaining 145 were nulliparas. The chief indications for curettage in this series were menometrorrhagia and sterility. Clinical experimentation was the sole reason for curettage in a smaller group of patients (Table I).

Some very interesting data relative to current gynecologic problems were gathered which differ from those uncovered in hospital practice. For instance, 4 of the 5 adenocarcinomas were at such an early stage of development that examination of the uterus following panhyster-

TABLE I. ANCILLARY DATA AND CONDITIONS INDICATING CURETTAGE IN 305 PATIENTS

Ages: 19 to 64 years	
Parity: Nulliparas 143	
Primiparas 58	
Multiparas 102	
CONDITIONS	NO. PATIENTS
Menometrorrhagia	163
Sterility	109
Amenorrhea	11
Induced hyperestrinemia (postmenopausal)	10
Premenstrual tension	8
Breast hyperplasia	4

ectomy showed no trace of the lesion. Likewise, the early elimination of malignancy as a diagnostic possibility by office curettage in the premenopausal bleeding group permitted a mode of treatment other than the application of radium which is the usual procedure in hospital practice and which is so frequently followed by severe castration symptoms. Although not germane to the subject under discussion, the endometrial findings in the several groups subjected to curettage are presented because of the current interest in endometrial physiology.

ENDOMETRIUM IN MENOMETRORRHAGIA

The menometrorrhagia in 96 of the 163 patients curetted was of the dysfunctional type. The causes of the abnormal uterine bleeding in the remaining 67 were widely diversified (Table II). The endometrial findings in the 96 patients with dysfunctional uterine bleeding (Table III) confirm, in the main, the observations of others (Burch,⁹ Campbell,¹⁰ Hamblen,¹¹ Kurzrok and Wilson,¹² Rock and Bartlett,¹³ and Payne¹⁴ and others) that there is no uniform endometrial pattern in this condition. In this series of 96 cases of dysfunctional uterine bleeding, the endometrium was hyperplastic in 67.7 per cent, proliferative in 17.7 per cent, atrophic in 9.3 per cent, and secretory in 5.3 per cent. It is, thus, apparent that endometrial hyperplasia is not a necessary accompaniment of dysfunctional uterine bleeding. Computation of the exact incidence of hyperplasia in any series of dysfunctional uterine bleeding depends on the histopathologic concepts of the observers and the time relation-

TABLE II. CAUSES OF ABNORMAL BLEEDING IN 163 PATIENTS SUBJECTED TO CURETTAGE

CAUSES	NO. PATIENTS
Dysfunctional	96
Cervical erosion (5) }	28
Cervical polyps (23) }	
Fibroids	11
Estrogen-induced (postmenopausal)	9
Ovulation bleeding	6
Adenocarcinoma	5
Dysfunctional, unrelieved by intrauterine irradiation	5
Incomplete abortion	2
Senile (atrophic) vaginitis	1

ship between the onset of the bleeding and the diagnostic curettage. In the absence of changes in the capillary walls or disparity in the size of the glands, it is often difficult to distinguish between a proliferative (interval) and an exaggerated proliferative (hyperplastic) endometrium. Moreover, it is of no special importance to make this distinction, inasmuch as the pathogenesis of the abnormal bleeding in both types of endometria is similar—prolonged, though not necessarily excessive, production of estrogen, unantagonized by the corpus luteum hormone, progesterin. The varying degree to which different portions of an endometrium may respond to the same hormonal stimuli is well-illustrated in the present series. No less than 16 of the 96 endometrial specimens obtained during the course of dysfunctional bleeding showed mixed patterns of hyperplasia, atrophy, and the secretory phase (Table III). The endometrial picture in dysfunctional bleeding is not appreciably influenced by the age of the patient, except in instances of atrophy which occur most frequently in postmenopausal women.

The interesting finding of a premenstrual (secretory) endometrium in 5 patients with dysfunctional uterine bleeding (Table III) supports the recent contention of Traut and Kuder⁷ that irregular shedding of the functional layers may be the immediate cause of prolonged or excessive bleeding.

ENDOMETRIUM IN FUNCTIONAL STERILITY

The complete dependence of human reproduction on the integrity of the endometrial cycle is too well-known to require elucidation. However, not until recently did gynecologists appreciate the importance of

TABLE III. ENDOMETRIAL PATTERN IN 96 PATIENTS WITH DYSFUNCTIONAL UTERINE BLEEDING

ENDOMETRIUM (Obtained during bleeding)	NUMBER	PERCENTAGE
Hyperplastic	49	51.0
Hyperplastic with patches of atrophy or premenstrual response (mixed pattern)	16	16.7
Proliferative (interval)	17	17.7
Hypoplastic (atrophy)	9	9.3
Premenstrual (secretory)	5	5.3

endometrial studies in functional sterility. Based on the studies of Heape,¹⁵ Hartman¹⁶ and Corner¹⁷ on the seasonal anovulatory bleeding of monkeys, several investigators¹⁸⁻²¹ have shown that its counterpart, pseudomenstruation, exists in the human female. This form of cyclic uterine bleeding, clinically indistinguishable from normal menstruation, occurs from an endometrium without secretory (nidation) changes. Elsewhere²² it was shown that pseudomenstruation is one of the important factors in the etiology of barren marriages. The diagnosis of this condition in regularly-menstruating sterile women rests on a study of the endometrium obtained prior to or at the very beginning of menstruation. For this reason, premenstrual curettage is a valuable part of our armamentarium in the study and treatment of sterility.

Of the 109 regularly-menstruating sterile women curetted premenstrually in the course of diagnostic studies, 36 (33 per cent) showed a total absence of the secretory phase. In 18 the endometria were proliferative, in 13 hyperplastic, and in 5 hypoplastic. In the light of our present knowledge concerning the factors involved in pseudomenstruation, the latter group with hypoplastic endometria were presumably ovulating and luteinizing, but their uteri failed to respond to the ovarian stimulus.

Primary dysmenorrhea was an additional complaint in 15 of the 109 sterile women subjected to a premenstrual curettage. In view of the current interest in the probable endocrine origin of dysmenorrhea and in view of the fact that the presence of a secretory endometrium implies an intact pituitary-ovarian mechanism, the endometrial findings in this group are especially noteworthy. Only 5 (33.3 per cent) of the 15 endometria failed to show the normal secretory phase, an incidence of pseudomenstruation no greater than in the entire group of sterile women. We must, therefore, conclude, in agreement with Lackner²³ and others, that there is no definite relationship between dysmenorrhea and the endometrial pattern.

THE ENDOMETRIUM IN AMENORRHEA, PREMENSTRUAL TENSION, AND IN ABNORMAL BREAST HYPERPLASIA

Realizing the hazard of drawing conclusions from observations on small groups of patients such as these 3 conditions represent in this report, we herein merely stress certain salient features of general interest.

Eleven amenorrheic women were curetted for the purpose of determining the functional state of the endometrium in relation to the estrogen content of the blood and urine. The latter was subthreshold or acyclic in 7 women and normal in 4. The endometrium in 6 of the 11 amenorrheic women was proliferative to a degree comparable to that seen in pseudomenstruation. The patients were, nevertheless, amenorrheic, indicating the correctness of Hartman's theory²⁴ of the existence of a bleeding factor, which was apparently absent in these patients. The endometrial specimens of the remaining 5 amenorrheic patients showed hypoplasia. It is interesting to note that 1 of the 5 patients with atrophic endometrium had never menstruated (primary amenorrhea) but, nevertheless, showed a normal level of estrogenic substance in both blood and urine, pointing to the presence of a congenital defect in the Müllerian tract. The endometrium of this patient, moreover, subsequently failed to respond to more than one-half million rat units of estrogen given during a period of two months.

This phenomenon, congenital or acquired nonresponsiveness of the endometrium, was further illustrated by the endometrial atrophy found in 7 of 10 postmenopausal women (Table I) who were receiving huge doses of estrogen (10,000 rat units in oil, given intramuscularly every fourth day for a period averaging four months) for the control of severe menopausal symptoms. The remaining 3 of the group of 10 women curetted during or at the termination of treatment showed an estrogen

response in the endometrium, proliferation (interval phase) in 2 and hyperplasia in the remaining 1. Irrespective of the endometrial response, not one of the 10 patients bled either during or after withdrawal of treatment, again stressing the apparent independence of uterine bleeding from the presence or absence of estrogen. Another group of 9 postmenopausal women (Table II) who were also receiving large doses of estrogen for the control of constitutional symptoms did develop abnormal uterine bleeding. These observations emphasize the fact that the question of the bleeding factor in its relationship to blood-estrogen levels is not yet unequivocally clarified.

Eight regularly-menstruating women with premenstrual tension (Frank²⁵), a relatively uncommon syndrome, characterized by a cyclic alteration of personality, were curetted premenstrually. The endometrial specimens of 4 of the 8 women were of the expected secretory type but those of the remaining 4 were proliferative or hyperplastic (pseudomenstruation). Inasmuch as pseudomenstruation often results from partial or total failure of luteinization, its frequent occurrence in premenstrual tension suggests that the syndrome, in some instances, may be related to an aberration of the normal ovulatory process.²⁶

Four regularly-menstruating women with abnormal breast hyperplasia (2 with generalized hypertrophy and 2 with adenosis) were subjected to premenstrual curettage in an attempt to evaluate the probable hormonal imbalance. The endometrium of the 2 patients with generalized hypertrophy showed no signs of progestin stimulation. Furthermore, 1 of these 2 patients showed double the normal quantity of blood and urine estrogen. These findings are corroborative of the present conception that generalized hypertrophy of the breasts results from a hyperestrinemia without the modifying influence of progestin. The endometrium of the remaining 2 patients who had multiple, painful nodules in both breasts, a condition known as adenosis or mazoplasia, was of the normal secretory type. Inasmuch as adenosis is attributed to a hyperfunctional state of the anterior pituitary lobe (Mazer,²⁷ and Lewis and Geschickter²⁸), a normal progestin-stimulated endometrium should be expected premenstrually in such women.

CONCLUSIONS

1. Study of the endometrium in 305 patients who were subjected to office curettage because of menometrorrhagia, functional sterility, amenorrhea, premenstrual tension, or abnormal breast hyperplasia furnished valuable information concerning probable etiology and uncovered 5 early cases of adenocarcinoma.

2. In the series of 305 office curettements herein reported, only 2 untoward reactions, temporary in nature, occurred.

3. Office curettage, carefully performed by the gynecologist, is a safe and valuable procedure.

REFERENCES

- (1) Kelly, H. A.: *AM. J. OBST. & GYNEC.* 9: 78, 1925. (2) Klingler, H. H., and Burch, J. C.: *J. A. M. A.* 99: 559, 1932. (3) Lörincoz, B.: *München. med. Wehnshr.* 6: 215, 1934. (4) Novak, E.: *J. A. M. A.* 104: 1497, 1935. (5)

Randall, L. M.: Proc. Staff Meet. Mayo Clin. 11: 58, 1936. (6) Bartelmez, G. W.: Contributions to Embryology, Carnegie Institution of Washington 24: 143, 1933. (7) Traut, H. F., and Kuder, A.: Surg. Gynec. Obst. 61: 145, 1935. (8) Mazer, C., Israel, S. L., and Kacher, L.: Ibid. 65: 30, 1937. (9) Burch, L. E., and Burch, J. C.: AM. J. OBST. & GYNEC. 25: 826, 1933. (10) Campbell, R. E., Lendrum, F. C., and Sevringhaus, E. L.: Surg. Gynec. Obst. 63: 724, 1936. (11) Hamblen, E. C.: Endocrinology 20: 769, 1936. (12) Kuržrok, R., and Wilson, L.: AM. J. OBST. & GYNEC. 31: 911, 1936. (13) Rock, J., and Bartlett, M. K.: J. A. M. A. 108: 2022, 1937. (14) Payne, F. L.: AM. J. OBST. & GYNEC. 34: 762, 1937. (15) Heape, W.: Phil. Trans. Roy. Soc. 188: 135, 1897. (16) Hartman, C. G.: Contributions to Embryology, Carnegie Institution of Washington 13: 161, 1932. (17) Corner, G. W.: J. A. M. A. 89: 1838, 1927. (18) Mazer, C., and Ziserman, A. J.: Am. J. Surg. 18: 332, 1932. (19) Tietze, K.: Arch. f. Gynäk. 155: 525, 1934. (20) Bland, B. P., First, A., and Goldstein, L.: J. A. M. A. 105: 1231, 1935. (21) Anspach, B. M., and Hoffman, J.: AM. J. OBST. & GYNEC. 28: 473, 1934. (22) Mazer, C., Israel, S. L., and Charny, C. W.: Pennsylvania M. J. (In press.) (23) Lackner, J. E., Krohn, L., and Soskin, S.: AM. J. OBST. & GYNEC. 34: 248, 1937. (24) Hartman, C. G., Firor, W. M., and Geiling, E. M. K.: Am. J. Physiol. 95: 662, 1930. (25) Frank, R. T.: Arch. Neurol. & Psych. 26: 1053, 1931. (26) Israel, S. L.: J. A. M. A. 110: 1721, 1938. (27) Mazer, C.: Med. Rec. 140: 417, 1934. (28) Lewis, D., and Geschickter, C. F.: J. A. M. A. 109: 1894, 1937.

2116 SPRUCE STREET.

21ST and SPRUCE STREETS.

DISCUSSION

DR. FLOYD KEENE.—The advantages to the patient of office curettage and its value as a means of diagnosis in both functional and organic disease are incontrovertible. Acceptance or rejection of this procedure depends upon whether it can be carried out with the same degree of safety and thoroughness as obtains with the patient under anesthesia in the hospital. In answer to this, the authors report their experience in 305 patients. Complications occurred only twice: Perforation of the uterus in one and a mild infection in the other. In 258 patients, the curettage was employed in the course of functional studies, and in 47, there was organic disease of the uterus, cervix, or vagina. Among the latter, there were 5 cases of adenocarcinoma, 4 of these lesions being so early that no cancer was found in the extirpated uteri.

In the face of such evidence, adverse criticism of a procedure with which I have had no experience would be presumptuous. This is not my purpose, but rather to state my reasons for not adopting it up to the present time. In my practice, one of the chief obstacles to the performance of office curettage without anesthesia would be the patient herself. If, to this lack of cooperation, one adds the frequent mechanical difficulties which render instrumentation impractical or unsafe, the number of patients in whom the procedure could be carried out becomes very limited. In this series of cases, the commonest indication for office curettage was endometrial biopsy in the course of functional studies. Granted that different portions of the endometrium do not show the same response to hormonal stimulation, I believe that in most instances this can be accomplished more safely, just as satisfactorily, and certainly more easily for both the patient and the surgeon by one of the cannulas now available.

When a diagnostic curettage is indicated, it should be performed in such a manner as to insure the maximum of safety, thoroughness, and accuracy. That these requirements can be met more expeditiously with the patient under general or spinal anesthesia in a hospital, seems to me so obvious as to require no further comment.

DR. BROOKE M. ANSPACH.—My own feelings in regard to this interesting proposal are very much the same as those expressed by Dr. Keene.

Another disadvantage of curettage as an office procedure occurs to me. When the curettings suggest malignant disease, one may, in the hospital, at a moment's notice obtain sufficient radium thoroughly to flood the endometrial cavity of the uterus with the gamma rays while the laboratory prepares rapid paraffin sections and makes a positive diagnosis. The advantages of such facilities are self-evident. Diagnostic curettage if it is to be of real value must be done thoroughly with a minimum of trauma and all aseptic precautions. I would favor the hospital.

DR. CATHARINE MACFARLANE.—I have not performed curettage in the office, nor do I wish to do so. I have done it twice in the operating room without anesthesia and regretted doing this, because the patients suffered severely and I felt at the time that I had not thoroughly curetted the uterus.

DR. ISRAEL (closing).—It is virtually impossible to persuade women with functional menstrual disorders to submit to hospitalization simply for diagnostic purposes. The possibility of accurate diagnosis in such instances is one of the major advantages of office curettage.

We are accustomed to performing diagnostic curettage, usually without anesthesia, in the Out-Patient Department of the Mount Sinai Hospital and, while we occasionally experience difficulty, we are usually able to pass the small fenestrated curette with ease. We have employed the suction-curette and have found it totally inadequate for our purposes. We do employ the Randall cannula-curette with satisfactory results. However, the cannula-curette causes as much pain and is only 2 mm. smaller than the No. 1 Sims curette.

RUPTURE OF THE GRAAFIAN FOLLICLES. II

JOSEPH T. SMITH, M.D., CLEVELAND, OHIO

WITH THE COLLABORATION OF ROSE C. KETTERINGHAM, B.S.

(From the Maternity Hospital, and the Department of Obstetrics and Gynecology, Western Reserve University)

INTERESTED in the phenomenon of the rupture of ovarian follicles as exhibited in the Friedman (rabbit) pregnancy test, we undertook to follow the sequence of events by examining the ovaries every two hours after the injection of the urine from a known pregnant woman. Careful study of the follicles at these various stages soon focused our attention upon the so-called "Bodies of Call and Exner,"^{1, 2} situated among the granulosa cells in the follicle walls. It appears to us that the changes in these organs run through a definite series before the rupture, and that the "bodies" play an important part in the phenomenon. Naturally, not all of the "bodies" seen will undergo these changes. For some reason, only a few of the hundreds of follicles present are at a stage of development that will permit them to respond to the stimulus of the urine injection. Only "bodies" in the walls of these few follicles will show the changes we describe. In other follicles, the "bodies" will remain quiescent.

Fig. 1 shows a normal, ripe human follicle, cut straight through the ovum, and showing a Call and Exner body in the base of the discus.

In Fig. 2 appear ripe follicles in the unstimulated rabbit ovary. Under this low magnification, many Call and Exner bodies appear, mere white spots scattered among the granulosa cells.

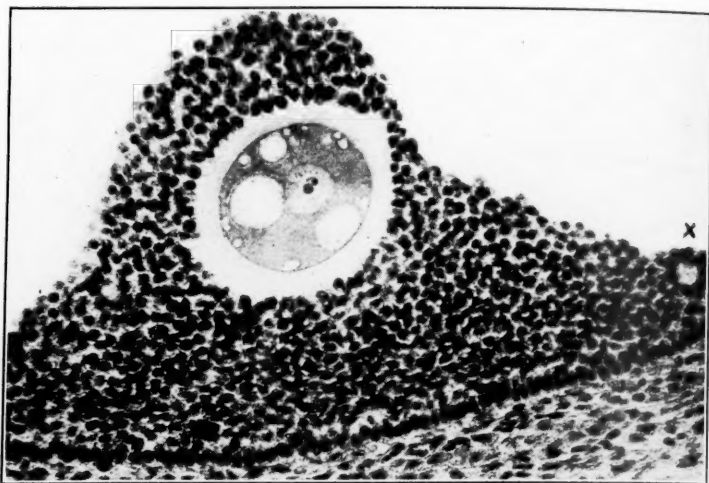


Fig. 1.—Human ovum in situ in follicle. Call and Exner body at X.

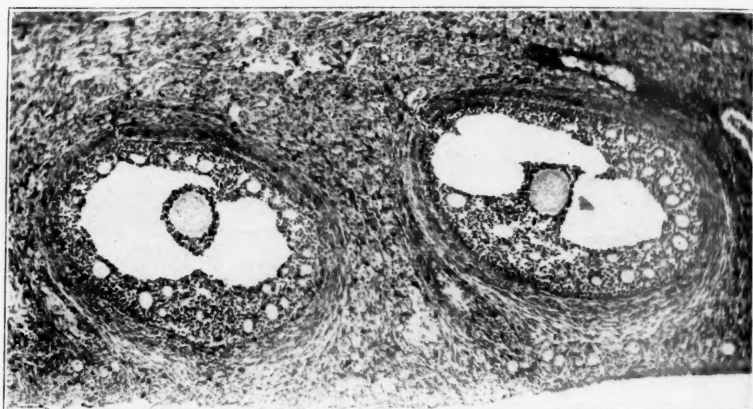


Fig. 2.—Follicles, unstimulated rabbit ovary. Call and Exner bodies.

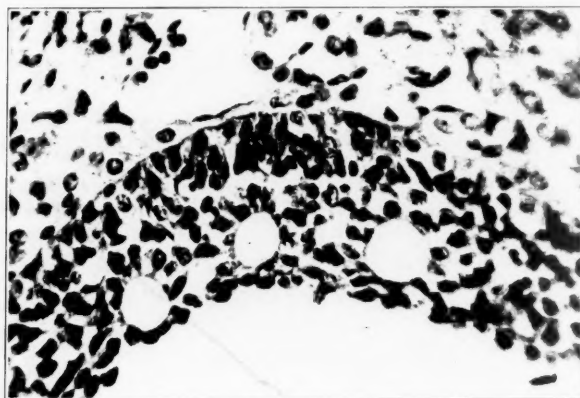


Fig. 3.—Call and Exner bodies; rabbit ovary, two hours after injection of urine of pregnant woman.

Fig. 3 is a higher power view of the "bodies" two hours after the rabbit had received an injection of urine. These "bodies" appear as amorphous spots, closely surrounded with the darkly staining nuclei of granulosa cells. No reaction seems to have started as yet.

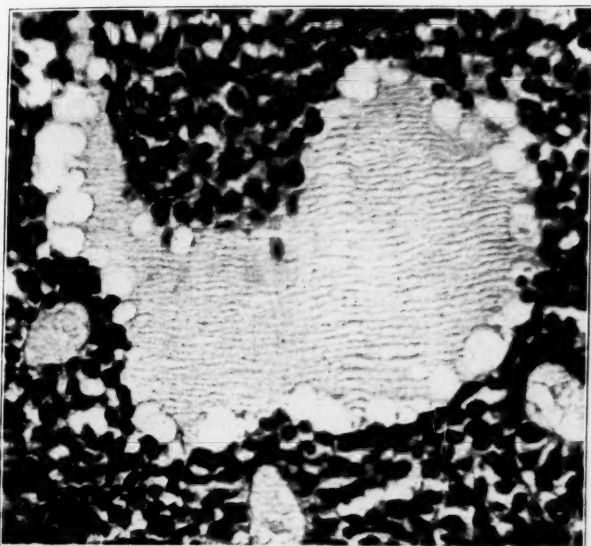


Fig. 4.—Call and Exner bodies, four hours after urine injection.

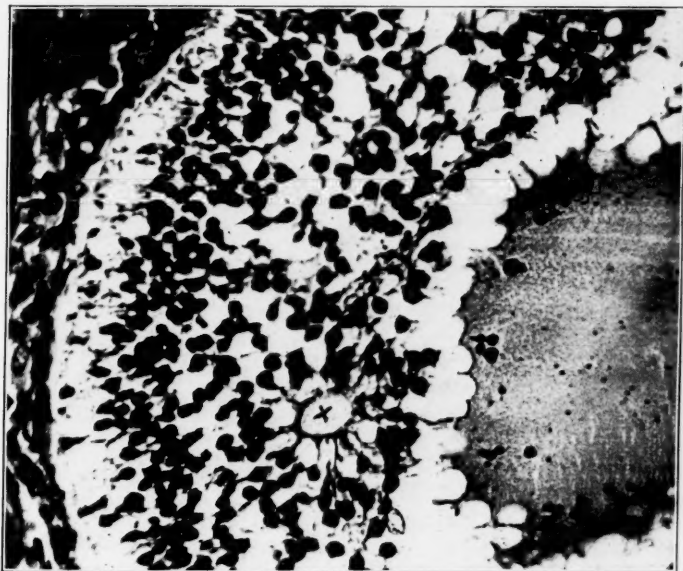


Fig. 5.—Call and Exner bodies, six hours after urine injection.

Fig. 4, taken four hours after urine injection, shows definite reticular structure in the "bodies." They appear larger, and their shape is more irregular. Granulosa cells are still packed closely around them.

In Fig. 5, the "body" appears to be freeing itself from the surrounding granulosa cells. Their nuclei are separated quite widely from the wall of the "body," and apparently there is an open moat between the "body" and the cells. This section was taken six hours after the urine injection.

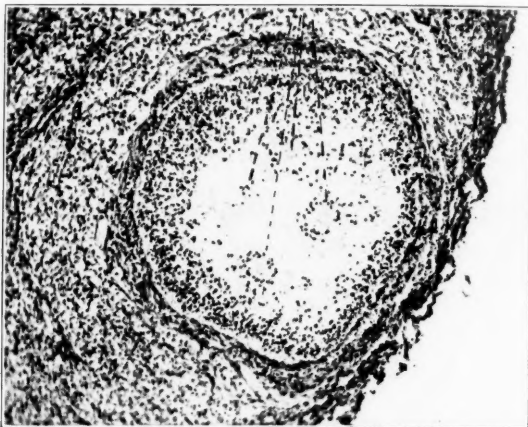


Fig. 6.—Low power view of follicle eight hours after urine injection. Broken lines point to Call and Exner bodies migrating into follicle fluid.

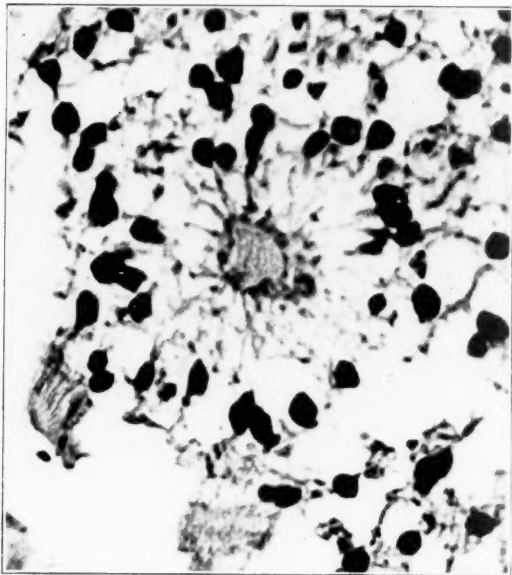


Fig. 7.—Higher power, same Call and Exner body, eight hours after injection of urine.

Fig. 6 is a low power view of a follicle eight hours after the urine was injected. Here we note that the "bodies" have cast loose entirely from the granulosa, and have moved toward the center of the follicle. Some of the surrounding cells cling to them, but have been pushed far off.

Seen under higher power, in Fig. 7, rays appear to emanate from the "body"; its margin is broken and irregular; it gives the appearance of undergoing disintegration.

We have examined many sections from the ovaries of rabbits which have not been stimulated by the injection of urine containing the prolans. In none of these slides can we find any Call and Exner bodies which present the picture seen eight hours after injection.

After eight hours, no trace of these "bodies" can be found in the follicles. Has their substance been entirely absorbed into the general follicle fluid?

Now it is just about this time, eight hours after stimulation, that a follicle begins to show definite swelling; an increasing internal tension which progresses until the rupture which occurs from ten and a half to twelve hours after the urine has been administered.^{3, 4} We felt justified in adopting the working hypothesis that these dissolving "bodies" have contributed something to the follicle fluid which increases its osmotic tension so that it takes up fluid from the surrounding tissue and so increases the content of the follicle until it reaches the bursting point. Previous observations⁵ have led us to believe that there really is such an increase of osmotic tension.

What could the Call and Exner body throw into the follicle that would thus raise the fluid osmotic tension? A salt or a sugar was our first idea. So we made a rough trial-and-error guess at the possibility that the sought-for substance might be a hydrocarbon. Follicles at the various stages were sectioned and stained with Best's carmine, which is said to be specific for glycogen. The results gave evidence that there really is some increase in the glycogen content of the "bodies" as the follicle approaches rupture.

The idea suggested itself that it might be possible to keep the blood sugar so low by the use of insulin that these "bodies" could not obtain the glycogen they need to perform their rôle in the rupture of the follicle, and thus the typical Friedman reaction might be inhibited. The matter has been tried out on a number of rabbits, using each time a control which received the same dose of the same urine as did the test animal, but which did not receive any insulin. During the tests, the blood sugar of both test and control rabbits was estimated frequently. Great difficulty has been met in our effort to keep the blood sugar at a uniformly low level for a period of about forty-eight hours. Attempts to keep it down frequently resulted in hypoglycemic shock for the animal. The giving of glucose at such a time will save the animal's life at the cost of pushing the blood sugar to too high a level. Many times, the blood sugar got out of control, and rose to an almost normal figure before the fact was detected at the next sugar estimation test. A very few hours of such near-normal are sufficient to vitiate an experiment.

Test Rabbit 1 lived twenty-seven hours, finally dying in insulin shock. Its blood sugar had been held down fairly well to figures ranging from 34.7 to 50 mg. per 100 c.c. The control rabbit, receiving no insulin, ran a blood sugar between 65 and 74. Organs were removed at once, after the death of the test animal, from it and from the control. They are pictured in Fig. 8. The control specimen, on the left, shows a strongly positive Friedman reaction. There are engorgement and hyperplasia of the uterine cornua, and many *corpora hemorrhagica* are seen in the ovaries. The test animal's organs, shown on the right, present no reaction what-

ever. The cornua are unengorged; the ovaries contain only mature but unruptured follicles. The black specks on these ovaries, seen in the photograph, are merely the cut ends of vessels entering the hila. The test animal and the control were litter mates, each weighing 2.94 kg.

In a second trial, we were so anxious to avoid insulin shock that we did not get the blood sugar of the test animal below 80. The animals were opened after forty-eight hours. Both the test and the control gave strongly positive reactions.

Experiment 3 also failed because, for some unexplained reason, the control rabbit as well as the test one failed to show any reaction.

At our fourth trial, the test rabbit died in shock too soon, at the end of eleven hours. Her ovaries showed no reaction at all. There was definite engorgement of the cornua of the control. There were no ruptured follicles; but sections showed the Call and Exner body changes we have described. This phenomenon was not seen in the test animal.



Fig. 8.—On right, uterus and ovaries from rabbit which received urine from a pregnant woman, and also insulin. No Friedman reaction. On left, uterus and ovaries of control animal which received the same dose of the same urine, but no insulin. Strong Friedman reaction.

In Experiment 5, the test animal was killed after twenty-eight hours, to avoid giving glucose for insulin shock. The sugar had been kept down pretty well, ranging from 94 to 37. A previous injection of glucose for shock had shot the blood sugar to 147. Here, too, the control gave a strongly positive Friedman reaction. The test animal showed little sign of change, though there was a trace of blood in the fluid of two unruptured follicles.

Trial six was also handicapped by failure to keep the blood sugar of the test animal at a uniformly low level. Glucose had to be given to counteract shock. The rabbit was kept alive forty-eight hours. Again, the control was strongly Friedman positive. The ovaries of the test animal showed, grossly, two follicles that appeared freshly ruptured. However, slides from the control showed masses of fresh luteal tissue growing into the follicles, whereas in the test animal not a trace of corpus luteum formation could be found.

In our seventh attempt, four rabbits were used. One was the control. We gave what, on the basis of the weights, we estimated to be about 1, 2/3 and 1/2 lethal doses of insulin to the three test animals. The rabbit receiving the heavy insulin dosage went into hypoglycemic shock frequently, and had to be rescued with glucose injections. These sent the blood sugar readings so high at times that they may explain the final atypical reaction in the ovaries, where some blood was found in one unruptured follicle. The other two rabbits showed no reaction, though the control gave the definite picture of a twenty-four-hour positive Friedman test. All the animals were opened twenty-four hours after the first urine injection because Rabbit 1 died in shock at that time.

Thus we come to believe that the sugar metabolism is an important factor in ovulation. Hyperglycemia may operate, as well as hypoglycemia. Diabetics are notoriously infertile. May it not be that, in them, the blood sugar raises the osmotic tension outside the follicle to a point so high that the contributions of the Call and Exner bodies are unable to concentrate the follicle contents to a point where fluid will pass in from the surrounding tissues?

It was suggested that a rabbit with a blood sugar reduced to about 50 is a rather ill animal. May it not be that, with its metabolism so low, many physiologic processes, such as ovulation, are inhibited? If its vitality were reduced by means other than insulin, might not the result be the same? In order to answer these questions, a rabbit, injected with urine from a pregnant woman, was twice reduced to the point of collapse by bleeding; once from the jugular, and once by needling the ventricle. In spite of this shock, the ovaries, at the end of forty-eight hours, showed a strongly positive Friedman reaction.

The blood sugar determinations were made by the micromethod of Folin and Malmros as modified for small amounts of blood by Jeghers and Myers.⁶ The technique was standardized as far as possible by having all blood collected and all tests run by the same person; satisfactory checks were obtained in practically all tests.

The ear of the rabbit was shaved to expose the marginal vein, which was punctured with a Hagedorn needle to obtain the sample. The rabbits bled freely from such punctures, and in most instances enough blood (50 c.mm.) was obtained for duplicate determinations. Occasionally the same puncture could be used for determinations at intervals of several hours by scraping off the small clot which formed following cessation of bleeding. Rabbit blood clots more quickly than that of human beings, especially if it comes in contact with fur, so it was necessary to shave a considerable area. Precautions in cleaning the ear were also of some importance, especially following the injection of 50 per cent glucose, since relatively small contaminations affect the validity of this sensitive test.

The normal fasting blood sugar for human beings by the Folin-Malmros modified test ranges from 70 to 90 mg. per 100 c.c. We have not determined the normal fasting blood sugar of rabbits by this method, since we were not primarily interested in this problem. As our animals were not uniformly fasted either before or during the tests, our figures represent only the determination for an individual rabbit at the time of test. Regardless of the blood sugar value at the beginning of the test, the majority of animals went into shock with values of 30 to 40 mg. per 100 c.c., although some individual differences were evident, just as in tolerance of insulin.

CONCLUSIONS

1. In the process of ovulation, in rabbits, the Call and Exner bodies of the follicle walls undergo characteristic alterations, and migrate toward and into the follicle fluid, where they disintegrate.

2. There is evidence that these "bodies" contribute something, possibly glycogen or a sugar, to the follicle fluid. This so raises the osmotic tension of the fluid that the follicle tension is increased to the point of rupture.

3. This idea of the mechanism is supported by observations that holding down the blood sugar with insulin definitely inhibits the rupture of the follicles.

We wish to express our gratitude to Dr. Arthur H. Bill for his interest and cooperation in this work. He made it possible for us to obtain the material needed for these experiments.

REFERENCES

- (1) *Thomson*: J. Anat., London 54: 1, 1919. (2) *Call and Exner*: Sitzungsber der Wien. Akad. LXXI, 1875. (3) *Regaud and Dubreuil*: Compt. rend. Soc. de biol. 64: 552, 1908. (4) *Smith*: AM. J. OBST. & GYNEC. 27: 728, 1934. (5) *Idem*: Ibid. 33: 826, 1937. (6) *Jeghers and Myers*: J. Lab. & Clin. Med. 15: 982, 1930.

10515 CARNEGIE AVENUE

HYPEREMESIS GRAVIDARUM*

A CLINICAL STUDY OF 396 CASES

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THE following report is based on the cases admitted to the Cook County Hospital during the twelve years from 1925 to 1936 inclusive. In that time 360 women were admitted to the wards because of vomiting that seemed intractable enough to require hospitalization. Of these, 29 were readmitted one or more times because of recurrent symptoms. The admission diagnosis was made entirely on the history given by the patient. Many patients were sent in from our own prenatal clinic, a certain number were referred by outside physicians, but the majority applied for admission because of their discomfort. This class of patient very rarely accepts hospitalization without good reason. No attempt was made to classify these cases as to their theoretical etiology.

Because there are no standardized criteria by means of which the seriousness of this condition may be estimated we have grouped the cases according to their hospital stay, hoping thereby at least to distinguish between those who responded readily to treatment and those who were more difficult to manage. It will be noted that nearly half of the patients were discharged in a week or less and that over two-thirds were well enough to go home by the tenth day, leaving less than one-third who were under treatment for more than ten days.

Theoretically, parity, color, and marital state may have some importance as etiologic factors in this condition. It has been stated that the disease does not occur in full-blooded negroes, and while many of our colored patients are not pure stock, nevertheless they accounted

*Presented at a meeting of the Chicago Gynecological Society, October 22, 1937.

TABLE I

Total number of patients	360
Number of admissions	396
ADMISSIONS	NO. OF PATIENTS
<i>Re-Entries:</i>	
2 X	23
3 X	5
4 X	1
<i>Days in Hospital:</i>	
7 or under	191
8-10	89
11 or more	116

for almost one-third of the patients. Similarly hyperemesis is supposed to be more common in unmarried patients. In this group they accounted for 10 per cent of the total, and this is about the same ratio as the unmarried group bears to the whole clinic. Two-thirds of our patients were multigravidas, and this is about the percentage of multigravidas in the entire clinic.

The diagnosis of this condition presents no difficulty. Many of the cases were very mild, but because of home responsibilities these patients object to hospitalization, and we are convinced that the diagnosis of

TABLE II. CLASSIFICATION OF PATIENTS

	NO. OF PATIENTS
Colored	117
White	212
Not recorded	28
Mexican	2
Japanese	1
Primigravidas	102
Multigravidas	248
Not recorded	10
Married	325
Single	35

hyperemesis was justified whenever they were willing to enter the hospital for treatment. No attempt was made to group them in accordance with the probable etiology of their symptoms. We have no record of any case which was relieved by the correction of local conditions, such as uterine malposition or cervical pathology. Our experience with the so-called neurotic vomiting has convinced us that whether or not neurosis may be the cause of severe vomiting, the health and even the life of the patient depend upon one's ability to control the symptoms. It is our belief that these patients would be better served if they were divided into two groups: (1) Those who improve promptly on proper management, and (2) those whose symptoms and findings persist in spite of adequate treatment. The patients in the first group are never in any danger. Those in the second group are always potential fatalities. No attempt is made to group the subjects of this report in this manner

but in the succeeding charts, they are divided into those who were considered cured at the end of ten days and those who were uncontrolled by that time.

Admission Findings.—All of these patients were admitted because of persistent vomiting. The majority complained of abdominal or epigastric pain. It will be noted that of those who were able to leave the hospital in ten days approximately one-third showed abnormal pulse and temperature on entrance. Nearly half of them showed acetoneuria. Such findings were definitely more common in the group whose symptoms were harder to control.

TABLE III. ADMISSION FINDINGS

	10 DAYS OR LESS	OVER 10 DAYS
Total cases	280	116
Pulse 100 plus	95	67
Temperature 99° F. plus	92	50
Urinary Findings		
Albumin	46	30
Acetone	135	71
Diacetic acid	40	29

TABLE IV. TREATMENT

	10 DAYS OR LESS	OVER 10 DAYS
Total cases	280	116
Glucose		
None	165	43
100 or less	85	34
Over 100	30	39
Saline		
None	165	43
5,000 or less	102	50
Over 5,000	13	23

Treatment.—Hyperemesis is a disease whose true etiology is obscure. Consequently the treatment has been mostly empirical, and the varieties thereof have been almost endless. These patients suffer from dehydration, starvation acidosis and damage to the parenchymatous organs, notably the liver. Obviously no one can suggest a treatment which fits every case or any individual case. Titus and Givens, in 1923, made certain suggestions that have proved generally helpful. They believed that these patients suffered from dehydration, loss of glycogen storage, toxic damage to the liver and possibly other organs. Experimental studies had proved that the liver of laboratory animals would withstand toxic doses of metallic poison such as phosphorus, provided the animal was given intravenous glucose as a buffer. They also showed that liver tissue damaged by such drugs as phosphorus or chloroform would regenerate with great rapidity in the presence of an excess of glucose in the blood stream. They suggested that hyperemesis, being a toxic process, would be benefited by the use of intravenous or subcutaneous glucose, because (1) fluids would be replenished, (2) the liver glycogen would be restored, (3) glucose would protect the liver from damage by toxin, and (4) glucose would enable the liver to repair its damaged areas more rapidly.

The patients here reviewed were treated individually by individuals. Practically every known form of treatment was utilized. Two general principles were agreed upon by the various staff members. One was that the use of fluids and glucose constituted a most valuable adjuvant to any other method of treatment. The other was that for the first twenty-four hours these patients should have nothing by mouth and be given proctoclysis of 5 per cent glucose in saline solution. Many of these patients showed prompt improvement with rest in bed, dietary restriction and rectal

feedings. Of those who remained ten days or less, practically 60 per cent had no further treatment, and of those who were not discharged in ten days, 40 per cent recovered on gastric rest and rectal feedings. The majority of these patients was readily controlled, and it is common knowledge that hospitalization and complete absence of visitors result in prompt improvement in most cases. In the more resistant cases, more strenuous treatment must be instituted. In this type of case, generous quantities of fluids and glucose were added to whatever other treatment the attendant deemed proper in the individual case. The additional fluid was normal saline solution given intravenously or subcutaneously. Glucose was given either in a 5 per cent solution subcutaneously or in 25 per cent solution intravenously. The general extent of this treatment is indicated in the chart. Obviously patients with more or less easily controllable symptoms received less intensive treatment. In the second group a third of the patients got more than 100 gm. of glucose contrasted to 10 per cent in the first group. Likewise 20 per cent of the second group were given more than five liters of fluid compared to less than 5 per cent of the first group.

The extent to which this treatment was carried in an effort to preserve the pregnancy and at the same time prevent harm to the mother can be illustrated by one case. This patient was a primigravida, aged 23 years, who entered in the fourth week of her pregnancy. On entrance she was referred to surgery as an intestinal obstruction because of abdominal distention with a history of incessant vomiting for ten days. After ruling out an obstruction she was transferred to obstetrics. On admission to our service the patient showed a pulse of 104 and a temperature of 99.8° F. Acetone and diacetic acid were present in the urine. The diagnosis was evident, but because she had taken ergot in an attempt to abort herself, the presence of a psychoneurosis was admitted as an etiologic factor. Treatment was instituted at once. During the next forty-three days fluids and glucose were given either subcutaneously or intravenously on thirty-four days. During that time this patient received 39 liters of subcutaneous saline. In addition she received 18 liters of 5 per cent glucose subcutaneously and 1,600 gm. of glucose in 25 per cent solution intravenously. Nevertheless her vomiting had not entirely ceased until the fortieth day, and acetone was present in the urine almost constantly for the same length of time. Her improvement was gradual thereafter and she was not discharged from the hospital until the seventy-fifth day. She was subsequently delivered of a normal infant at term.

TABLE V. ABORTIONS

Spontaneous	4
Therapeutic	32
Recovered	23
Died	9

TABLE VI. FATALITIES

Deaths	15
Pregnancy interrupted	9
Pregnancy not interrupted	6
Re-Entries	9
Discharged from OB as improved	3
Signed release	4
Discharged from Medical Service	2
Entered in terminal state	2
Entered with polyneuritis	2
Additional cases	2

Abortion.—In spite of treatment a certain number of these patients failed to improve. Thirty-two were subjected to therapeutic abortion. Of these, 23 recovered promptly and were discharged well. Nine died even though the uterus had been emptied. The details of these cases will be reported in the study of the fatalities of the series.

Deaths.—Hyperemesis is a disease which should never result fatally unless the patient is fatally damaged when first seen. The occurrence of 15 deaths, even in a large series of cases and over a long period of time requires comment and explanation if we are to eliminate this disease as a factor in maternal mortality.

Of the 15 fatal cases in this group, four patients entered the hospital for the first time with such marked damage that there was never any possibility of help from any method of treatment. Two of them entered with a pulse over 120, temperature over 101° F. Both were irrational. Both had involuntary urination and defecation. One died in fifty hours, the other early in her fourth hospital day. Two patients entered with definite peripheral polyneuritis. One of these had been treated for four weeks in another hospital and was transferred to us because she had become irrational and had visual and auditory hallucinations. She had stopped vomiting and was taking food by mouth. Because of this apparent improvement relatives refused permission to empty the uterus. In spite of large quantities of glucose and fluid the patient became worse, and permission to empty the uterus was obtained on the fourth day. There was no improvement, and the patient died on the ninth day. The other patient with polyneuritis was aborted on the third day, but in spite of this and generous quantities of fluid and glucose she died on the eleventh day. These 4 patients entered the hospital too late for treatment.

One patient was treated in a medical ward for eight days as a pelvic peritonitis. She was then transferred to us with a pulse of 124, temperature 99° F., albumin, acetone and diacetic acid in the urine. This patient was treated medically for fourteen days, during which time she received 400 gm. of intravenous glucose, 100 gm. of subcutaneous glucose and 16,400 c.c. of saline. In spite of the fact that her temperature remained normal, her pulse remained well over 100, and her urine continued to show acetone and diacetic acid. She was becoming listless and uncooperative and the uterus was emptied on the twenty-second hospital day. Treatment was continued, but there was no response. She died on the thirty-second day. This patient, we feel, could have been saved by earlier abortion.

One other patient entered with normal temperature, pulse of 104 but with albumin, diacetic acid and acetone. On the third day casts appeared in the urine. On the fourth day a bag was inserted (she was four months pregnant). In spite of generous quantities of glucose and fluid, she continued to get worse. On the sixth day she was irrational and on this day she expelled the fetus. She died on the ninth day. The lack of promptness in aborting this patient is open to criticism.

Nine of the 15 deaths are of particular interest, because the patients had been in the hospital previously during their current pregnancies. Seven of these had been in the obstetric ward because of vomiting. Four left the hospital on their own responsibility. One returned after seventeen days in terminal condition, bleeding from the nose and mouth; red cell count was 1,100,000, pulse 130, temperature 101.8° F. Dilatation and curettage were done on the third day and the patient died on the fifth day.

Two others of this group re-entered after twelve days. One was retaining food and fluids but was listless, sluggish, and uncooperative. On the eighth hospital day she became irrational, and the uterus was emptied. She died ten hours later. Earlier abortion might have prevented this fatality. The other patient who returned in twelve days received the usual intensive treatment and on the seventh day was thought to have a pneumonia. The uterus was never emptied, and she died on the seventeenth day. This death should have been preventable. The last of this group re-entered after eight days. She had an active gonorrhea, which made the wisdom of a therapeutic abortion questionable. In addition to this she was in a ward reserved for the treatment of venereal disease, and the seriousness of her toxemia was underestimated. Therefore, the severe vomiting was allowed to continue almost without treatment. By the fifth day she had become irrational, but she had stopped vomiting. The next day she was able to retain food, but she was stuporous and irrational. She died on the fifteenth day. It seems reasonable to believe that this patient could have been saved by early and proper treatment.

Three patients had been released from the Obstetrical Wards as improved or cured. One returned in fifteen days in terminal condition and died in forty-eight hours. Another returned in twenty-eight days and died in thirty-six hours. The other returned in nine days, with a pulse of 150, temperature 101° F., albumin, acetone and diacetic acid. She was aborted on the seventh day and died on the tenth. It is evident that these patients were not cured when they were allowed to leave the hospital on their previous visits. Of the two who were released by the medical service, one was discharged as pregnancy with cholelithiasis and given dietary management. She returned in seventeen days vomiting but with negative urine, a pulse never over 120 at any time. She developed periods of irrationality and the vomiting was persistent in spite of negative laboratory findings. She was not aborted until the twenty-first day and she died on the twenty-second. The other was discharged as a duodenal ulcer because of a previous history. She was sent back to the hospital nine days later by the prenatal clinic, but her vomiting was slight and she was considered a threatened abortion. Her pulse remained around 120 but her temperature and urine were normal until the fifteenth day. On the sixteenth day she was curetted by the resident on the Obstetrical Service and a loop of bowel was pulled out through a perforation in the uterus. She died on the operating table in an attempt to repair the damaged bowel.

COMMENT

Consideration of a large number of cases of hyperemesis reveals that they may be placed in two groups for prognostic study. The first group improves readily, often with no treatment except rest and isolation, and the life of the patient is never in jeopardy. The smaller second group responds slowly to treatment and is responsible for a small number of maternal deaths. The deaths from this disease could be decreased by a more widespread recognition of its potential seriousness. A study of the fatal cases of this series indicates that a certain number of deaths might have been prevented, and that they can be prevented in the future by close attention to some general principles:

1. The so-called cured patients should be kept under close observation.
2. The lack of clinical improvement, regardless of laboratory findings should be regarded as a bad prognostic factor.
3. Likewise, apparent clinical improvement such as cessation of vomiting and ability to retain food, in the presence of persistent tachycardia, elevated temperature and persistent urinary abnormalities, may give one a false idea of the patient's improvement. In 6 of the 15 fatal cases the patients were retaining food for some time before death.
4. Listlessness, stupor, involuntary urination and defecation, and periods of irrationality are frequently evidence that the toxemia will result fatally whatever the treatment.
5. The use of cervical packs, bags, etc., is not recommended in cases where therapeutic abortion is to be done. If the cervix is not easily dilatable, vaginal hysterotomy should be done so that the uterus may be emptied promptly.

SUMMARY

1. Three hundred ninety-six cases of hyperemesis are reviewed.
2. There are 32 therapeutic abortions.
3. There were 15 deaths in this series.
4. Color, age, parity, and marital state seem to have no influence on the course of the disease.
5. Persistent tachycardia, fever, diacetic acid, and acetone are danger signals.

6. Ability to retain food and fluids in seriously ill patients is not necessarily a sign of improvement.

7. Deaths from hyperemesis are avoidable.

8. The majority of this group responded promptly to rest, diet, glucose therapy, and fluids.

9. Those that fail to respond to adequate treatment in a reasonable length of time should be aborted.

10. Therapeutic abortions delayed too long are not life-saving measures.

104 SOUTH MICHIGAN AVENUE

30 NORTH MICHIGAN AVENUE

DISCUSSION

DR. FREDERICK H. FALLS.—There are several special types of this disease. One group which was not mentioned presents symptoms of hyperthyroidism. We have had a considerable number of these cases showing basal rates varying from plus 111 to 140. These patients have lost a great amount of weight, have a fine tremor, a pulse of 120, and enlargement of the thyroid. They are the women who if they were not pregnant would be diagnosed Graves' disease. If you give these women Lugol's solution, 10 drops, three times a day throughout pregnancy, the vomiting is controlled. These cases have been seen in consultation by men skilled in thyroid surgery, who have made a diagnosis of hyperthyroidism and advised thyroidectomy. They have believed that such patients would improve over a short period of time and then, if not operated upon, would develop a thyroid crisis. In pregnancy, however, under medical management this does not occur. One woman for instance took Lugol's solution from September 26 until February 3, when she was delivered. Her thyroid symptoms subsided almost immediately. She was then sent to the same surgeon who had advised thyroidectomy during her pregnancy, but he now could find no need for an operation.

There is a group also due to intestinal obstruction, especially following an appendectomy with drainage. One woman of 23 years had had an appendectomy with drainage at the age of nine years. She became pregnant two years ago and had to be aborted because of the hyperemesis. She became pregnant again this year and developed all the symptoms of hyperemesis gravidarum plus the symptoms of partial obstruction. When she came to us the question was whether we should attempt to enter the abdomen and relieve the obstruction in the presence of severe hyperemesis, jaundice, dehydration, and with diacetic acid in the urine, or empty the uterus again. We felt we did not dare to subject her to this risk and instead emptied the uterus.

I would like to re-emphasize what Dr. Fitzgerald said about polyneuritis and also about mental symptoms. I remember one patient with severe hyperemesis, who was found wandering about the halls at night slightly irrational. We later did a vaginal hysterotomy under local anesthesia. She lost about two ounces of blood, but her pulse went from 160 to 210. We returned her to bed and gave hypodermoclysis. Her pulse came down to 160 but she died on the second day. We had a complete post mortem except the thyroid and that was not thought to be important at that time. The pathologist could not tell us from what this woman had died. The liver and kidneys failed to show the usual degeneration said to be characteristic of this disease.

After emptying the uterus many of these patients are not saved. In two other instances on my service in Iowa, the patients lived a month after the uterus was emptied. One patient was taking an adequate diet but she died of toxemia. The other patient continued to vomit for a month and died. I feel there are things about this disease that are not understood, and that some of these cases are associated with hyperthyroidism.

DR. EDWARD L. CORNELL.—In the management of these cases, we often forget that vitamin B and other vitamins are necessary to prevent polyneuritis. Vitamin extracts should be included in the diet.

Many of us neglect also to use the Levine tube for feeding these patients. You can often succeed in getting food in the duodenum by this means.

Glucose, 10 per cent solution, should be given in amounts of at least 3,000 c.c. intravenously in the first forty-eight hours. After that, if the toxicity is diminishing, the 5 per cent solution will be adequate.

RELATIONSHIP OF ORAL THRUSH TO VAGINAL MYCOSIS AND THE INCIDENCE OF EACH

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THIS study was undertaken to determine the relationship of the sporadic cases of oral thrush in the newborn to vaginal mycosis in the mother, and the general incidence of each. This work was stimulated by the lack of adequate data supporting the views expressed in the literature. A series of routine vaginal cultures on 402 women in the third trimester of pregnancy was taken to determine the incidence of fungi. Also a series of 90 babies with positive oral thrush was studied with relationship to mycoses in their mothers. It will be shown later that the incidence of fungi in the genital tract of the mothers appears to be associated with the hygienic level, further that the babies born of such infected mothers have about a thirty-five times greater chance of developing oral thrush than infants born of noninfected mothers.

For a rather complete review of the literature the reader is referred to the study by Plass, Hesseltine, and Borts¹ on "Monilia Vulvo-vaginitis."

The reported incidence of yeast vaginitis varies; Haussmann² in 1875 reported that 11 per cent of women in late pregnancy harbored the organism without symptoms; v. Winkel³ in 1866 found six cases of mild infection among 150 women, an incidence of 4 per cent; v. Herff⁴ noted 24 cases of acute, and subacute mycotic vaginitis among 13,283 admissions, an incidence of only 1 in 553, and of these 15 occurred among 2,010 pregnant women (1 in 134) while the remaining 9 occurred among 11,273 gynecologic patients (1 in 1,252). The last author excluded from his series, however, those patients who showed obvious evidence of mycotic vaginitis, as determined by the presence of thrushlike patches on the vaginal mucosa. In the study of 63 patients with symptoms, by Plass, Hesseltine, and Borts,¹ 18 were pregnant, and 45 nonpregnant; an incidence of 66.7 per cent was found in the pregnant group, and an incidence of 24.4 per cent in the nonpregnant group. In a control series of 85 patients without symptoms of irritation, among 46 pregnant patients an incidence of 32.6 per cent was found, while in 39 nonpregnant women the incidence was 15.4 per cent. It was concluded that economic status did not influence the occurrence, and that the increased percentage among the pregnant patients was partially explained by the known preference of mycotic organisms for an acid media, which is present in the vagina in pregnancy. Stander⁵ quotes that "yeasts" were

found in 25 per cent of pregnant women at term by cultural methods. Recent literature reveals only a few articles, and most of our textbooks pay little attention to vaginal mycosis, thus explaining the paucity of observations on the incidence of fungi in the vagina.

Too little attention has apparently been shown toward the possible source of oral thrush in the infants from mothers infected with mycotic vaginitis. Haussmann² demonstrated, immediately after birth, spores in the mouths of children born of mothers with vaginal mycosis. Noack, Faber and Clark, and Cron⁶ have all stated the possibility of oral thrush being due to genital infection of the mother. More recently Crossen⁷ pointed out that a mother might infect herself, and a vaginal mycosis result from her thrush-infected baby. DeLee⁸ states that one may have a yeast vaginitis which resembles oral thrush. Very few authors have called attention to the danger of infection of the newborn by the yeast infection of the mother. Hesselstine, Borts, and Plass⁶ proved by experimental inoculation that the fungi present in the vaginas of pregnant women can produce oral thrush. This has been confirmed recently by the excellent study of Bland, Rakoff, and Pincus.⁹

PROCEDURE

Research work was carried out in the Chicago Lying-in Hospital and the Stock Yards dispensaries. The patients who attend the hospital clinic are of a definitely better economic class than those in the Stock Yards clinic. In the latter, the patients were segregated into two groups, white and colored, while at the former no colored patients are accepted. Cultures were taken as routinely and consecutively as possible, being only interrupted by certain unavoidable factors. Each patient was asked about the presence of genital symptoms and observations were made on the amount of vaginal discharge and clinical appearance. A culture was then taken from the vagina with a sterile swab and implanted on Sabouraud's media, the cultures incubated for twenty-four to forty-eight hours and then read.

In the study of oral thrush in the babies, the charts were reviewed from the opening of the new Lying-in Hospital in May, 1931, up to Oct. 31, 1936. Undoubtedly some records of babies with oral thrush were missed in this review, especially those for the earlier years. The clinical diagnosis was confirmed in each case by direct smears and/or culture. Then the records of all mothers of babies with oral thrush were reviewed to check the relationship of the possible mother's infection to the baby's thrush. In addition to the above groups, there was a similar study on 47 mothers with positive culture for fungi and on their 47 babies.

DISCUSSION

In Table I we quote the further unpublished results of Plass, Hesselstine, and Borts which were presented in the Scientific Section Exhibit at the American Medical Association convention in Philadelphia in 1931.

TABLE I

PREGNANT PATIENTS		YEAST	
		PRESENT	ABSENT
(No symptoms)	184	60 (32.6%)	124 (67.4%)
(With symptoms)	48	27 (56.25%)	21 (43.75%)

These authors found that among the 232 pregnant women studied, yeast organisms were found by culture and/or smear in 87 patients, a total incidence of 37.5 per cent. Of this positive group only 27, or 11.63 per cent, of the total had symptoms and evidence of a vulvovaginitis. Of the 87 pregnant patients who had positive evidence of mycosis 27 (or 32 per cent) had symptoms.

The findings in our series of 402 women who were examined during the third trimester of pregnancy for evidence of vaginal mycosis are shown in Table II.

TABLE II

CASES	LOCATION		POSITIVE {SMEARS CULTURES		NEGATIVE {SMEARS OR CULTURES
100	Stock Yards Colored	With symp.	17 (17.0 %)	41.0 %	5 (5.0 %)
		Without symp.	24 (24.0 %)		54 (54.0 %)
150	Stock Yards White	With symp.	25 (16.66%)	33.33%	5 (3.33%)
		Without symp.	25 (16.66%)		95 (63.33%)
152	C.L.I.H.	With symp.	8 (05.26%)	14.47%	5 (3.28%)
		Without symp.	14 (09.21%)		125 (82.89%)

The three groups of patients have been reviewed separately because of their different hygienic standards. The white and colored groups from the Stock Yards clinic are almost entirely indigent patients from the lower classes, while the Lying-in series of 152 cases are from a much better hygienic and social state. Of these groups, the indigent colored group shows a total incidence of 41 per cent, and the indigent white group an incidence of 33 per cent, while the nonindigent, or Lying-in group, shows an incidence of only 14 per cent. This apparently contradicts some earlier voiced opinions as to the influence of the economic level and personal hygiene of the patients. Taking the total number of patients with vaginal mycosis, regardless of class, which is 113 out of the series of 402 cases, the total incidence is 28 per cent. Of the 113 patients with positive evidence of mycosis, only 50 had symptoms of a vulvovaginitis, or 12.4 per cent of the total group. Or, on the other hand, 50 of the 113 patients with evidence of mycosis had symptoms, an incidence of 44.2 per cent.

Of the babies born to 152 women in the Lying-in group, 3 developed oral thrush, all three mothers having had positive cultures for vaginal mycosis; thus in this series the incidence of oral thrush was 1.98 per cent. Here 100 per cent of their mothers had vaginal mycosis.

Among 44 mothers not studied elsewhere who had positive evidence of vaginal mycosis, 7 babies developed oral thrush, or 15.9 per cent. Adding the above three mothers to the latter 44, a total of 47 positive mothers showed an incidence of oral thrush in their babies amounting to 21 per cent.

From the opening of the present hospital on May 25, 1931, until Nov. 31, 1936, among approximately 14,640 babies delivered, 90 babies developed oral thrush (Table III). Thus, approximately 1 baby among 162 developed oral thrush in our entire service, an incidence of 0.6 per cent. Some records of cases of oral thrush may have been missed during the earlier years.

TABLE III. THE INCIDENCE OF ORAL THRUSH FOR EACH FISCAL YEAR OF THE HOSPITAL

YEAR	NO. CASES OF ORAL THRUSH
5/25/31 to 6/30/31	0 (?)
7/ 1/31 to 6/30/32	1 (?)
7/ 1/32 to 6/30/33	6 (?)
7/ 1/33 to 6/30/34	17
7/ 1/34 to 6/30/35	22
7/ 1/35 to 6/30/36	39
7/ 1/36 to 10/31/36	5
5½ years	90 cases

TABLE IV. THE INCIDENCE OF ORAL THRUSH IN THE NEWBORN

	NUMBER	NO. ORAL THRUSH	INCIDENCE
Babies born	14,640	90	0.6%
Mothers with known vaginal mycosis	47	10	21.0%

From Table IV, therefore, one may conclude that a baby born of a mother with known vaginal mycosis has approximately a 35 times greater chance of developing oral thrush than a baby born of a mother without a known mycosis in the Chicago Lying-in Hospital.

TABLE V. DATA CONCERNING THE MOTHERS OF THE 90 BABIES WITH ORAL THRUSH

Mothers with positive yeast cultures (genital)	22
Mothers with negative yeast cultures	27
Mothers with no cultures taken	41

Among the mothers of these thrush-infected babies, it was found that 49 had been studied either ante partum, post partum, or both (Table V). Of these 49 mothers 22, or 44.89 per cent, were found to have positive evidence of vaginal mycosis, while 27, or 56.11 per cent, had no demonstrable evidence of the infection.

TABLE VI. DISTRIBUTION OF THE BABIES WITH ORAL THRUSH TO THE NURSERIES

	CASES OF THRUSH	AVERAGE NO. BABIES IN NURSERY (PER DAY)
Second floor nursery	10	15
Third floor nursery, south	45	25
Third floor nursery, north	25	25
Fourth floor nursery	8	12
Isolation nursery	2	8

The time at which the cases of oral thrush developed was noted also. These factors could not be determined accurately in some of the earlier cases, so that they were omitted in forming the following conclusions. Of 66 cases of thrush among approximately 6,130 babies, 43 were probably endemic, and 23 were questionably contracted by contagion in the nurseries. Thus, we might say the incidence of thrush to all babies in this series is one in 92, or 1.07 babies out of 100 will have thrush.

CONCLUSIONS

1. The incidence of fungi in the vagina of women in the third trimester of pregnancy is 28 per cent.

2. The incidence of fungi in the vaginal tract appears to be related to the economic level and personal hygiene of the patient; indigent colored patients show an incidence of 41 per cent, indigent white patients an incidence of 33 per cent, while the more hygienic class of white patients shows an incidence of only 14 per cent.

3. The incidence of oral thrush in the newborn shows a definite relationship to the presence of fungi in the generative tract of the mother. At the Chicago Lying-in Hospital a baby born of a mother harboring fungi in the vagina has about a 35 times greater chance of developing oral thrush than a baby born of a noninfected mother.

4. Among 14,640 consecutive babies delivered at the Chicago Lying-in Hospital the incidence of oral thrush was found to be 0.6 per cent. However, in the last 6,130 babies of this total number the incidence of oral thrush was about 1 per cent. This apparent increase we feel is only the result of more careful observations.

REFERENCES

- (1) Plass, E. D., Hesselstine, H. C., and Borts, I. H.: AM. J. OBST. & GYNEC. 21: 320, 1931. (2) Haussmann, D.: Parasites des organes sexuels femelles de l'homme et de quelques animaux, avec une notice sur le développement de l'Oïdium Albicans Rob, J. B. Baillière et fils, Paris, 1875. (3) v. Winckel, F.: Berl. Klin. Wehnschr. 3: 237, 1866. (4) v. Herff, O.: Samml. Klin. Vortr. Gynäk. n. F., 34-67, 1894-1897. (5) Stander, H. J.: Williams Obstetrics, ed. 7, New York, 1936, D. Appleton-Century Company, Inc. (6) Hesselstine, H. C., Borts, I. H., and Plass, E. D.: AM. J. OBST. & GYNEC. 27: 112, 1934. (7) Crossen, H. S., and Crossen, E. J.: Diseases of Women, St. Louis, 1935, The C. V. Mosby Co. (8) DeLee, J. B.: The Principles and Practice of Obstetrics, ed. 6, Philadelphia, 1933, W. B. Saunders Co. (9) Bland, P. B., Rakoff, A. E., and Pincus, I. J.: Arch. Dermat. & Syph. 36: 760, 1937.

Heynemann, T.: Operative Treatment of Puerperal Sepsis, Deutsche Ztschr. f. Chir. 248: 198, 1936.

Main consideration in the treatment of puerperal sepsis is removal of the septic focus through exposure and drainage or through extirpation of a suppurating organ. The localization of such foci constitutes the real problem in treatment of puerperal sepsis. Vein ligation is seldom indicated. It is to be considered only in cases in which sepsis is of thrombophlebitic origin. The operation of vein ligation is technically not difficult; the real difficulty lies in the uncertainty of its indications. Hysterectomy is not indicated in treatment of sepsis. The only exceptions to this rule are gas bacillus infection of the uterine musculature and, occasionally, an infected myoma or abscess of the uterine wall in the course of the puerperium. These complications, however, are unusual. Hysterectomy is likewise to be considered in certain cases of life-threatening hemorrhages developing in the course of a febrile puerperium or due to retained placental tissue.

J. P. GREENHILL.

PULMONARY TUBERCULOSIS IN AN ACTIVE OBSTETRIC SERVICE

WITH AN ANALYSIS OF 15 CASES

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IN THE past several years much has been said and written of pregnancy and parturition associated with pulmonary tuberculosis, especially in regard to whether or not these physiologic functions have any ill effect on tuberculous women. Most, if not all, of the reported statistics have emanated from various tuberculosis sanatoria. This analysis was undertaken with the view of presenting the role of pregnancy and parturition in pulmonary tuberculosis from the standpoint of an active obstetric service in a general hospital.

In a study of 19,634 consecutive deliveries in St. Catherine's Hospital from Jan. 1, 1918 to Dec. 31, 1935 there were found to be 15 associated with pulmonary tuberculosis, an incidence of one in every 1,309 deliveries.

As shown in Table I there were 11 cases of active pulmonary tuberculosis as evidenced by history, physical signs, positive sputum, x-ray findings, and clinical course.

TABLE I. CASES OF ACTIVE TUBERCULOSIS

CASE	AGE	PARITY	TYPE OF DELIVERY	HOURS IN LABOR	KNOWN DURATION TB. PROCESS AT TERM	POST-PARTUM COURSE	FOLLOW-UP
1	33	iii	Prem. 7 mo. Ret. placenta	4	Developed post partum	Died 18 days p.p.	-
2	26	ii	L.O.A. low forceps	10	3 years	Normal	Unknown
3	25	iv	Spont. L.O.P. P.P. hem.	10	3 months	Febrile	Unknown
4	31	v	Spont. R.O.A.	12	Discovered at term	Died 3 weeks p.p.	-
5	27	i	Premature 7 mo.	5	1 year	Febrile	Died 2 mo. p.p.
6	33	ii	Spont. R.O.A.	4	Developed old tb. hip	Febrile	Died 2 years p.p.
7	27	i	Spont. R.O.P. Ret. placenta	9	6 months	Febrile	Died 3 mo. p.p.
8	32	i	L.O.A. low forceps	4	6 months	Died 6 days p.p.	-
9	21	i	Spont. L.O.A.	17	Developed p.p.	Febrile	Unknown
10	34	v	Spont. L.O.A.	3½	3 months	Febrile	Died 3 mo. p.p.
11	23	i	Low forceps R.O.A.	8	Discovered at term	Died 1 hour p.p.	-

In Table II there are shown 4 cases of inactive or chronic pulmonary tuberculosis as determined by history, physical signs, negative sputum, x-ray findings, and clinical course.

TABLE II. CASES OF INACTIVE TUBERCULOSIS

CASE	AGE	PARITY	TYPE OF DELIVERY	HOURS IN LABOR	KNOWN DURATION TB. PROCESS AT TERM	POST-PARTUM COURSE	FOLLOW-UP
1	35	ii	Spont. L.O.A.	5	1 year	Normal	Living and well
2	26	ii	Spont. L.O.A.	7½	3 years	Normal	Living and well
3	27	i	Spont. R.O.A.	8	2 months	Normal	Living and well
4	24	ii	Spont. L.O.A.	7½	3 years	Normal	Unknown

Analysis of Tables I and II reveals that of the 11 active cases there were 7 patients who died within three months of delivery and which can reasonably be considered post-partum deaths, giving an immediate mortality rate of 64 per cent for the active cases, and a mortality for the entire series of 47 per cent including those cases where follow-up could not be obtained. Among the active cases there was one death two years post partum. There was apparently no ill effect in the cases of inactive tuberculosis.

Parity apparently had no influence, there being 6 primiparas and 9 multiparas; although one would expect to find a greater mortality among the multiparas due to the added strain of successive labors and the additional care of one or more children. The average age in this series was twenty-eight.

There was no evidence of any interference with labor itself. There were 12 spontaneous deliveries and 3 patients delivered by prophylactic low forceps. The average duration of labor in the primipara was nine and one-half hours, in the multipara six and one-half hours.

There are several very significant and somewhat astounding facts noted in this series. In 10 cases, or 66½ per cent, the onset of tuberculous symptoms began after pregnancy occurred and in 8 cases, or 53 per cent, the tuberculous process was not discovered until the onset of labor. None of the active cases received sanatorium care or any adequate treatment during the course of their pregnancy. At first glance this would seem to be a serious indictment against the type of prenatal care given these patients, but it may be that this is but another proof of the insidiousness of the tuberculous process and the manner in which pregnancy brings to the fore a latent pulmonic lesion.

A review of the literature reveals that little is known of the true incidence of pulmonary tuberculosis in pregnancy, and a perusal of vital statistics from the Department of Health of the City of New York sheds no further light. However, available figures tend to show that pulmonary tuberculosis is no more likely to occur in pregnant than in nonpregnant women.

There have been several schools of thought concerning the true effect of pregnancy on pulmonary tuberculosis. The early investigators¹ of this subject held that pregnancy exerted a favorable influence on its course. Later, the pendulum swung to the opposite direction and the opinion was well nigh unanimous that pregnancy was fraught with great danger to tuberculous women. In recent years, however, there have been several articles purporting to show that pregnancy has no effect on pulmonary tuberculosis.

Thus, Barnes and Barnes² in a study of 535 sanatorium cases concluded that pregnancy does not necessarily exert a deleterious effect on pulmonary tuberculosis. Similarly, Hill,³ and Jennings and others,^{4, 5} in their statistical studies reached the same conclusion. Ornstein and Kovnat⁶ in reporting a series of 85 cases from the Sea View Hospital state that pregnant women with tuberculosis fare as well as their nonpregnant tuberculous sisters. On the other hand, Matthews and Bryant⁷ in their

study of the obstetric histories of tuberculous women, formerly patients at Trudeau Sanatorium, find that pregnancy is definitely harmful, and Hill herself admits that the greatest mortality is found among the cases diagnosed after the termination of their pregnancy and the least in those known to have tuberculosis before the onset of pregnancy. In evaluating these reports it must be remembered that practically all of these cases are sanatorium patients, that the pregnancy occurred during the course of a known pulmonic lesion and that most of them received at least some sanatorium treatment. When we consider that 53 per cent of the cases in St. Catherine's, an average-sized general hospital with a large and active obstetric service, did not manifest themselves until term and that the known mortality was 47 per cent, and if we multiply these figures by the number of similar general hospitals throughout the country with undoubtedly the same experience, we will obtain results greatly at variance with the above reports. It would seem, therefore, the proper conclusion to be drawn from the above reports is that the prognosis of properly treated cases has improved and not that pregnancy per se has no ill effect on tuberculous women.

Most authorities are in agreement that the most dangerous periods for these women are during labor and the puerperium. The exact reason for this seems somewhat obscure. Certainly, however, the strain of labor with its attendant trauma and blood loss must play some part. It was formerly believed that the descent of the diaphragm with resultant sudden decompression of the pleural cavity at the end of the second stage of labor was the cause of flareups, but Jameson,⁸ in his exhaustive review of the literature of the entire subject states that this theory is untenable as the result of recent studies of the intrapleural pressure before and after delivery. He believes that the extension of the tuberculous process during labor or the puerperium is due to the increase of capillary permeability which is known to occur at this time.

It is well agreed that pulmonary tuberculosis per se has no effect on labor. The cases in the present series are in accord with this.

As regards the treatment of this condition, the profession is beginning to take a more definite stand. Formerly it was common practice to abort pregnant women as soon as the pregnancy was discovered.

This practice continued in vogue until 1926 when Bridgman and Norwood⁹ in reporting a series of 134 cases of tuberculosis in pregnancy found that in those cases where therapeutic abortions were performed 57 per cent died within a year after abortion. They concluded that therapeutic abortion has no place in the treatment of this condition and state "operative procedure in the presence of an active pulmonary lesion is followed by a higher mortality rate than if expectant therapy alone is employed." Barnes and Barnes in a study of 42 therapeutic and spontaneous abortions reached the same conclusion. They also condemn therapeutic abortion from another viewpoint because of the fact that 80 per cent of tuberculous pregnant women deliver a perfectly normal child.

The main dictum in the care of tuberculous pregnant women is "treat the tuberculosis and disregard the pregnancy." Close cooperation between the obstetrician and the phthisiologist is an absolute requisite for a successful outcome. In active cases a strict sanatorium regime with absolute bed rest is essential as soon as the pregnancy is discovered. In those cases where tuberculosis develops after pregnancy has occurred, the sooner the lesion is discovered the sooner rational therapy can be

instituted. For this reason the prenatal care in all pregnancies should include a careful chest examination and thorough investigation of any chest symptoms which may arise during the pregnancy.

Of late years, a powerful weapon has been added to the armamentarium in the battle against pulmonary tuberculosis, namely collapse therapy, especially artificial pneumothorax. Pneumothorax has been found to be especially fitted for use in pregnant tuberculous women and to give very gratifying results. However, it must at all times be remembered that pneumothorax is intended primarily to supplement sanatorium and bed rest therapy and not to replace them.

Such treatment should be continued until the onset of labor. Here every effort should be made to conserve the patient's strength and to minimize blood loss, trauma, and the chances of infection. With this in mind, certain clinics elect to perform a cesarean section. However, the shock of such a formidable procedure may result in a spread of the tuberculous lesion. The procedure of choice in conservative hands is the liberal use of sedatives to produce obstetric analgesia in the first stage of labor and as soon as the cervix is fully dilated, the application of forceps under local anesthesia, nitrous oxide or ethylene. Labor is made as easy and as short as possible. Obstetric complications are, of course, dealt with in the usual manner.

The patient having delivered, strict attention is again focused on the tuberculosis and the obstetrician and phthisiologist continue their close cooperation. The same regime is reinstituted as during the ante-partum period, and the use of pneumothorax is again brought into play. The mother is not allowed to nurse, since this has been found quite detrimental in pulmonary tuberculosis. Intensive treatment is continued until well past the puerperium when the case is turned over exclusively to the phthisiologist and further therapy is instituted as indicated.

CONCLUSIONS

1. Pregnancy has a definitely deleterious effect on active cases of pulmonary tuberculosis, especially in those cases in which the tuberculosis develops after pregnancy has occurred.

2. Careful attention should be paid to chest signs and symptoms during prenatal care.

3. In all cases of tuberculosis during pregnancy the patient should have strict sanatorium care and the use of artificial pneumothorax where indicated, plus the close cooperation of the obstetrician and the phthisiologist.

4. Delivery should be effected with a minimum of strain to the patient.

5. As a result of the modern conservative treatment of pregnant tuberculous women, the prognosis of this condition has definitely improved.

I wish to express my thanks to Dr. Charles A. Gordon whose kindly advice and many suggestions have made this paper possible.

REFERENCES

- (1) Norris, C. C.: Gynecological and Obstetrical Tuberculosis, New York, 1931, D. Appleton & Company. (2) Barnes, H. L., and Barnes, L.: *AM. J. OBST. & GYNEC.* 19: 490, 1930. (3) Hill, A.: *Am. Rev. Tuberc.* 17: 113, 1928. (4) Jennings, F. L., Mariette, E. S., and Litzenburg, J. C.: *Am. Rev. Tuberc.* 25: 673, 1932. (5) Jennings, F. L., and Mariette, E. S.: *Am. Rev. Tuberc.* 25: 687, 1932. (6) Ornstein, G. G., and Kovnat, M.: *Am. Rev. Tuberc.* 31: 224, 1935. (7) Matthews, H. B., and Bryant, L.: *J. A. M. A.* 95: 1707, 1930. (8) Jameson, E. M.: Gynecological and Obstetrical Tuberculosis, Philadelphia, 1935, Lea & Febiger. (9) Bridgman, E. W., and Norwood, V.: *Bull. Johns Hopkins Hosp.* 38: 83, 1926.

215 JEFFERSON AVENUE

A STUDY OF 738 CASES OF UTERINE BLEEDING IN CONDITIONS OTHER THAN PREGNANCY

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IN A series of 4,421 admissions on the gynecologic service of a general hospital between 1928 and 1936 inclusive, abnormal uterine bleeding in conditions unrelated to pregnancy was observed or complained of as a symptom in 738 cases (16.6 per cent). The existence of pregnancy, intra- or extrauterine, automatically eliminated the case from this study, though the bleeding may have been due to factors unconnected with the pregnancy. It is manifest that in any large series the cases do not always categorically group themselves under one or another single etiologic heading. Associated conditions are frequently present in addition to the major lesion. In classifying such associated lesions the major pathologic condition, the one which was obviously or probably responsible for most or all of the bleeding, determined our choice of heading.

FIBROMYOMA

Fibromyoma occurred in 340 cases, or 46 per cent of the series. As is seen from Table I, the greatest number of these cases were treated by supravaginal hysterectomy, a procedure which yielded a mortality rate of 2.6 per cent. In the course of most of these operations the ovaries were removed if the patient was in the menopausal or premenopausal age. As Table I indicates, the series treated by curettage and radium was smaller but there was no fatality. The indications and contraindications of surgical and radiotherapy need not be reviewed here. This fact, however, impressed us forcibly, viz., that the simplicity of administration, the wider margin of safety, and economy in time and money strongly favor the use of radium. Both hysterectomy and radium find their greatest field of usefulness about and after the menopause. The results with radium in properly chosen cases are good, objectively and subjectively. Its use should always be preceded

by curettage and the curettings should be routinely subjected to microscopic examination. Occasionally, malignancy will be thereby disclosed where hitherto unsuspected, as occurred three times in this series. Despite the fact that in this series supravaginal hysterectomy was the procedure most commonly used, analysis of the results and the considerations beforementioned lead one to believe that radium will narrow the field of major surgery in the treatment of the fibroid uterus. Its advantages do not appear to be generally appreciated.

TABLE I. METHODS OF TREATMENT AND RESULTS IN FIBROMYOMA

OPERATION	CASES	RE- COVERED	IM- PROVED	UNIM- PROVED	DEATHS
Curettage	23	7	16	0	0
Curettage and radium	27	8	19	0	0
Supravaginal hysterectomy	192	174	12	1	5 (2.6%)
Total hysterectomy	8	7	0	0	1 (12.5%)
Vaginal hysterectomy	12	12	0	0	0
Laparomyomectomy	75	69	4	0	2 (2.6%)
Vaginomyomectomy	3	3	0	0	0
Total	340	280 (82.3%)	51 (15%)	1 (0.39%)	8 (2.3%)

It is not, in our opinion, sufficiently employed in cases where no contraindication to its use exists. Fibromyomas larger than a 3½ months gravid uterus and those complicated by degenerative changes within the growths or pelvic inflammatory disease were considered unsuitable for radium therapy. It is recommended that, before hysterectomy is resorted to for fibromyoma, a contraindication to the use of radium in a given case be established. In the menopausal cases 1,500 mc. hr. of radium were given, thereby establishing a permanent amenorrhea. The symptoms of the artificial menopause thus induced have been no more disturbing than in the natural climacteric. A survey of the causes of death following hysterectomy for fibromyoma indicates that myocardial failure occurred in 2 patients, pneumonia in 2, pulmonary embolus in 1, and paralytic ileus in 1. There were no deaths in the patients treated with radium.

During the childbearing age myomectomy was the procedure of choice, reaching the peak in the third decade; hysterectomy was most frequently done about the middle of the fourth decade; and radium enjoyed its greatest use several years later in the same decade. In a few instances, though over 20 fibroids had been enucleated it was possible to reconstruct a functioning uterus with a subsequent menstrual cycle. In one of these instances the patient's decision as to whether or not to consummate marriage to her betrothed entirely depended on the possibility of conserving her uterus. Twenty-three fibroids were enucleated, the uterus was reconstructed, and marriage ensued. As she has been practicing contraception for the past three years, it is not possible to submit an opinion as to her fertility. One may be assured, however, that the psychic state of a patient who knows by her catamenia that she has not been unsexed is much healthier than

that of one who has been deprived of her uterus, ovaries, or both; and this, irrespective of whether she bears children or not. It follows, therefore, that much can be achieved in the way of conservation of structure in cases which at first glance appear insuperable.

ENDOMETRIAL HYPERPLASIA

Next in frequency to fibromyoma in this series as the cause of bleeding was endometrial hyperplasia which was the only discoverable abnormality in 175 cases out of a total of 738 cases, or 23.7 per cent, approximately half the incidence of fibromyoma. In each case the diagnosis was made by the pathologist after careful microscopic examination.

The treatment most commonly employed was simple curettage which yielded satisfactory results, particularly in the younger age group. In patients who were at or about the menopause, the curettement was supplemented by radium. Radium was not employed in younger subjects unless one or more previous curettages and an adequate trial of endocrine therapy had failed to check the hemorrhage. When used before the premenopause the dose was between 400 and 600 mc. hr.

In those cases of endometrial hyperplasia in which an associated condition requiring laparotomy existed, follicular cysts of the ovaries were uniformly found, a finding which accounts not only for the hyperplastic condition of the endometrium consequent upon persistent ovarian stimulation but for the excellent results achieved by radiotherapy. It appears, therefore, that in uncomplicated endometrial hyperplasia, hysterectomy is contraindicated.

The small number of cases (9 in 175) in which hysterectomy was done, were at or after the menopause. The indications were associated pathologic lesions or failure to respond to less radical treatment.

There was one death in this group following a curettage and excision of a cervical polyp. This occurred in a patient seventy-one years of age who had diabetes. Death occurred seventeen days postoperatively from myocardial failure.

TABLE II. METHODS OF TREATMENT AND RESULTS IN ENDOMETRIAL HYPERPLASIA

OPERATION	CASES	RE- COVERED	IM- PROVED	UNIM- PROVED	DEATHS
Curettage	102	76	25	0	1 (0.9%)
Curettage and radium	64	44	19	1	0
Supravaginal hysterectomy	8	7	1	0	0
Vaginal hysterectomy	1	1	0	0	0
Total	175	128 (73.1%)	45 (25.7%)	1 (0.57%)	1 (0.57%)

FIBROSIS UTERI

Next in frequency to endometrial hyperplasia as a cause of bleeding was fibrosis uteri which occurred in 68 of the 738 cases, or 9.2 per cent. In those patients in whom hysterectomy was done, the diagnosis

of "fibrosis" was made by the pathologist. In the other patients the diagnosis was made clinically by the presence of a uniformly enlarged, hard uterus in a subject generally about the menopause who suffered from meno- or metrorrhagia.

The method of treatment employed in young women (i.e., those in whom future childbearing is a factor) was simple curettage. If the bleeding recurred within a period of one to several years the curettage was repeated one or more times. Radium, even in small doses (400 to 600 mc. hr.), was used infrequently and reluctantly during the childbearing age, and only in patients who failed to respond to prolonged endocrine therapy and repeated curettage, and in whom the bleeding was severe enough to affect the general health. A castration dose was never given before the premenopause.

The most suitable patients for radium were those in the menopausal age. The symptoms of the artificial menopause thus induced were, as in the fibromyoma group, no more pronounced than in the natural change, while relief from anxiety over pregnancy (imaginary or otherwise) improved the psychic status appreciably. The results were good. Hysterectomy was less often resorted to in the menopausal group than radium. There were no deaths in the radium treated series as compared with one death in the hysterectomized group. It appears, therefore, that hysterectomy should be given second consideration in the treatment of this condition, and used only after radium has failed to control the bleeding unless there is associated pathology which requires laparotomy.

TABLE III. METHODS OF TREATMENT AND RESULTS IN FIBROSIS UTERI

OPERATION	CASES	RE- COVERED	IM- PROVED	UNIM- PROVED	DEATHS
Curettage	12	5	7	0	0
Curettage and radium	34	21	13	0	0
Supravaginal hysterectomy	19	15	3	0	1 (5.2%)
Vaginal hysterectomy	2	2	0	0	0
Total hysterectomy	1	1	0	0	0
Total	68	44 (64.7%)	23 (33.7%)	0	1 (1.45%)

MALIGNANT NEOPLASMS

The total number of malignant neoplasms was 28 in a total of 738 cases, or 3.7 per cent. There were 12 cases of carcinoma of cervix; 9 of carcinoma of corpus; 3 of sarcoma of corpus; 2 of carcinoma of ovary; 1 of sarcoma in fibroid; and 1 of granulosa cell tumor of ovary. The frequently observed lower incidence of carcinoma of the cervix in Jewish women is evident in this series. Although over 90 per cent of the patients in the entire series were Jewish, it was observed that the 12 cases of carcinoma of the cervix were equally distributed between Jewish and non-Jewish patients. Analysis showed that in the case of malignant neoplasms of the corpus and ovary no such relative racial

immunity existed. It is believed, however, that the series is too small to be conclusive in the latter respect.

The 28 cases of malignancy, according to decade incidence, were distributed as follows: 14 in fourth decade; 9 in fifth; 4 in third; and 1 in sixth decade.

OTHER CONDITIONS

Polyps occurred in 49 cases (6.6 per cent) of which 43 (5.8 per cent) were cervical and 6 were uterine (0.8 per cent). No instance of malignancy in a polyp was observed.

Chronic inflammatory disease as a cause of bleeding was noted in 24 cases (3.2 per cent). The bleeding, as a rule, was not the most prominent symptom in this group. Conservation of genital structure and function was held paramount in the treatment of the younger patients in whom, in fact, this lesion most frequently was observed.

Benign ovarian neoplasms occurred in 18 cases (2.4 per cent) of which 13 were cysts, 4 fibromas, and one a granulosa cyst.

Anatomic displacements as causes of bleeding were found in 29 patients (3.9 per cent). They responded well to plastic operations which reduced or eliminated tissue drag and circulatory embarrassment involving the ovary. In younger women preservation of the reproductive function, here as elsewhere, determined the choice of operative procedure. Retroversion in this class of patient was corrected by a round ligament operation after the method of Olshausen or Gilliam. When childbearing was no longer a factor, the Watkins interposition operation and tubal sterilization have proved satisfactory. Very rarely were vesical symptoms pronounced enough to militate against the value of the procedure. In recent years the Fothergill operation has been coming into increasing vogue. The results have been good.

There was one case of fibrosis of cervix and 2 of glandular hyperplasia of cervix in all of which the bleeding was not marked. Finally, there were 4 patients in the series in whom no lesion within or without the uterus could be found to account for the bleeding. Blood dyscrasia was ruled out. These cases were classified as of undetermined cause, probably endocrinopathic.

SUMMARY

1. In a series of 4,421 admissions on the gynecologic service of a general hospital, abnormal uterine bleeding due to conditions unrelated to pregnancy was present in 738 patients (16.6 per cent).

2. The commonest single cause of bleeding in the 738 cases was fibromyoma which occurred in 340 (46 per cent). Though supra-vaginal hysterectomy was the procedure most commonly employed, the impression gained has been that radium insertion on account of its safety, efficiency, technical simplicity and economy of time and money will narrow the field of major surgery in the treatment of the

fibroid uterus. Fibroids larger than a 3 and one-half months gravid uterus and those undergoing degenerative changes or complicated by pelvic inflammatory disease are not suitable for radiation.

3. Myomectomy, single or multiple, is the procedure of choice in younger women.

4. Next in frequency to fibromyoma as the cause of bleeding was endometrial hyperplasia which occurred in 175 patients (23.7 per cent). Simple curettage in younger subjects yielded good results in the vast majority of patients while curettage with radium insertion in the menopausal group yielded excellent results. Whenever laparotomy was performed for some complicating condition, follicular cysts of the ovary were observed in association with endometrial hyperplasia.

5. Next in frequency was fibrosis uteri which occurred in 68 patients (9.2 per cent). The best results were achieved in the menopausal group in which the treatment par excellence is curettage and 1,500 mc. hr. of radiation with the element inserted in the fundal area of the uterus. It is believed that hysterectomy should not be performed except in those rare instances in which radium has failed.

6. There was no fatality following the use of radium in fibromyoma, endometrial hyperplasia and fibrosis. With hysterectomy, the results were less favorable.

7. The total number of malignant neoplasms of the reproductive organs was 28 (3.7 per cent). A relative immunity to carcinoma of the cervix was noted in Jewish patients. No such immunity was evident with respect to malignant neoplasms of the corpus and ovary.

8. No instance of malignancy was observed in 49 polyps (6.6 per cent) of which 43 were cervical and 6 uterine.

Grateful acknowledgement is due to Dr. Leo Schwartz, Chief of Staff, for his cooperation in this survey as well as to the various staff members whose case records have been utilized. For the arduous task of arranging preliminary data credit is due to Messrs. H. Merenstein and H. Levy.

4506 TWELFTH AVENUE

Lash, A. F.: Surgical Treatment of Puerperal Sepsis, *Am. J. Surg.* 37: 68, 1937.

Surgical treatment should be utilized in certain types of puerperal sepsis in conjunction with medical treatment. These surgical cases can be determined by history, repeated examination and thorough and constant clinical study.

The operations employed by Lash were colpotomy, abdominal drainage and removal of diseased structures and hysterectomy, each operation being employed in certain pathologic states. Vein ligation has been done so rarely in the Cook County Hospital and the mortality in these patients is so low that the tendency now is entirely toward conservative management with repeated blood transfusions.

J. P. GREENHILL.

HYPERPYREXIA PRODUCED BY THE HOT BOX IN COMBINATION WITH THE ELLIOTT TREATMENT

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THE history of the beneficial effects of artificial fever in the treatment of gonorrhea is now well known due to the numerous papers published on this subject in the last five years. Hyperpyrexia is no doubt a major step forward in the care of this disease particularly in the female and even more especially when arthritis is associated with it. In the latter instance, it may perform miracles.

However, the treatment as originally performed by Carpenter and Warren¹ may be dangerous and can be trusted only in the hands of a few highly specialized workers. It requires the constant attendance of a physician and even in his presence, heat strokes and unavoidable sequelae may occur. This refers to the type of treatment in which a fever of 106.7° F. by rectum for periods of five to twenty hours or multiple treatments of shorter periods is induced by radiant heat in an enclosed space or hot box. In these cases restraints are necessary and the pulse rate reaches 160; the patient is frequently on the brink of a heat stroke and collapse. Experience with this method makes one conclude that it is far more dangerous than the disease.

Bishop, Lehman, and Warren² in their paper of a comparison of 3 electrical methods of producing hyperthermia show two charts with pulse rates continually ranging between 170 and 190 beats per minute at a temperature of 106.7° F. These authors have treated 111 patients, 64 females and 54 males, the single hyperpyrexia lasting from five to seventeen hours though less than the thermal death time of the organism with 80 per cent of them cured. A later report of 100 cases treated at the thermal death time gave 87 per cent cures and 1 death is reported. Desjardins, Stuhler and Popp³ cured 40 out of 45 patients by 2 to 4 treatments of five or six hours each. Bennett and Austin⁴ treated 16 patients in a similar manner and obtained 12 cures. Anderson, Arnold and Troutman⁵ cured 39 of 54 patients by this method, all the patients being males. It would appear from these reports that the treatment is efficacious and without particular danger.

In order to lower the pulse rate Simpson, Kislig and Littler⁶ were the first to appreciate the value of air conditioning the hot box, as the greater the saturation of the air with moisture, the less perspiration is evaporated on the skin surface, and therefore the less the cooling effect. Their results are the same as others though the patients are more comfortable. However, they report minor burns (vesicles) in about 3 per cent of the cases.

The "hot box" was used for one year at Bellevue Hospital following the original technique of Carpenter and Warren¹ and in spite of constant medical aid, we had three major calamities. One patient died from heat stroke and two others had severe heat strokes with resulting deep burns that necessitated skin grafting and long hospitalization netted only 55 per cent cures. Aside from the serious and fatal complications of this type of treatment, the discomfort to the remaining cases was so great that few patients would submit to more than one

treatment. Meanwhile, reports from other clinics stated that 4 to 6 treatments were not unusual for a cure, and it was felt that our failure to employ multiple treatments accounted for the low percentage of cures, namely 55 per cent.

Notwithstanding these poor results, it was believed that heat was the proper means with which to attack gonorrhea, and an attempt was made to perfect a technique which would eliminate the generalized dangers and discomforts and which still could be carried out in a simple fashion.

Such a treatment would seem to require a prolonged high pelvic temperature to kill the gonococci and a lower cerebral temperature, which would not kill or endanger the life of the patient. The higher the cerebral temperature the more symptoms of medullary stimulation will be exhibited by the patient—fast pulse, rapid respiration, vomiting and restlessness—and thus the patient comes nearer to a heat stroke and collapse. The lower the cerebral temperature the greater became the margin of safety and the greater the general comfort of the patient.

To obtain this happy medium, a regular hot box treatment was given, but the mouth temperature was maintained at 105° F., and at the same time a continuous Elliott treatment was carried out with the water in the vaginal bag at 115° F. The resultant temperature curves show the rectal temperature to be 2° to 2.5° F. higher than the mouth temperature during the treatment. By this method the rectal temperature is higher than the 106.7° F. induced by radiant heat alone in the discarded type of fever therapy; the general condition of the patients is never a cause for alarm after the first hour, when they exhibit slight restlessness. The pulse stays around 140 or lower; no restraints or heavy sedatives are necessary. The patient is under the constant care of a nurse trained in this work, and she calls for a staff doctor if any unusual symptoms occur. The former treatment necessitated the constant attendance of a physician; the present treatment requires his presence only until the fever reaches a maximum.

PROCEDURE

The technique is simple and suitable for the average hospital staff, not necessitating a special training in physiotherapy. The only contraindications to the treatments are: (1) Those patients who are running a temperature of 102° F. or over from salpingitis or other causes. One may except from this, patients with gonorrheal arthritis or septicemia. These patients should be treated as soon as possible. (2) Intact hymen, as it will not allow insertion of the vaginal bag. (3) General medical contraindications as heart disease, tuberculosis, etc.

The patient is given 3 gr. of sodium amytal the night before the treatment and an enema the following morning. When she is put in the hot box the body is covered with a blanket to increase the humidity around the skin surface and to prevent burns. The Elliott vaginal bag is inserted in the vagina and the cork is wound with cotton padding. The Elliott machine is set for 115° F. and runs automatically. Occasionally its temperature will go over 115° F. and must be lowered with ice water. The doors of the hot box are closed and the bulbs are turned on full. When the temperature reaches around 103° F. the patient becomes restless and $\frac{1}{6}$ of a gr. of morphine sulphate and $\frac{1}{200}$ of a gr. of scopolamine is administered by hypodermic. This is repeated in three or four hours. The mouth temperature is taken every ten minutes. Cold fluids should not be given just preceding this. The nurse holds the lips shut over the thermometer as the patient is usually drowsy. The

rectal temperature is taken every twenty minutes, and if it is more than 2.5° F. higher than the mouth temperature, the latter is very carefully rechecked. No alarm is felt for the condition of the patient unless the pulse is around 150 with a dropping blood pressure. She is given only water and orange juice to drink during this treatment. After six hours of maintained temperature of 105° F., the box is opened and the patient put to bed. It is important to check the temperature every twenty minutes for two hours after the treatment to make sure the temperature has dropped to normal, as heat stroke can occur after the cessation of the treatment.

Seventy-nine patients treated by the combination of hot box and Elliott treatment had a total of 148 treatments without any major complication. One patient showed impending symptoms of heat stroke one and one-half hours after the start of the treatment when her temperature was only 104° F. She gave a past history of encephalitis which undoubtedly made her heat sensitive. The treatment was stopped and she was never in danger, yet developed a mild burn in that short period of time. The treatment was stopped in 2 other instances because of the rate of pulse. No damage resulted, but these partially treated cases are included as failures.

Occasionally some patients will develop small blisters, especially about the lower abdomen and hips, but these are of no importance and do not occur if covered with a blanket. It is not uncommon to find blistering of the vagina from the Elliott bag, but this condition heals readily and never causes scars or strictures.

Of the 79 patients treated, 23 had only one treatment with 15 cures, while 50 patients had 2 treatments with 42 cures (84 per cent cured). Of 5 patients submitted to a third treatment 2 were cured. Only 1 patient had a fourth treatment and this resulted in a cure.

With one treatment, 15 patients were cured out of 23, showing that the thermal death time of the organisms not killed was over six hours at this particular height of temperature. Most of these patients refused to repeat the treatment or left the hospital. Even some failures, however, benefited to a certain extent, for 3 had negative cervical and 3 negative urethral spreads.

Forty-two out of 50 were cured by two treatments. Two of the failures occurred at the beginning of the series and were not carried out at maximum temperature and the entire second treatment was not completed, while the remaining failures can only be explained on their heat resistancy. This same explanation can account for the 60 per cent failures of the 3 treatment series, as demonstrated by the Rochester group of workers, Boak, Carpenter, Mucci and Warren^{7, 8} who have determined the in vitro thermal death time of 250 strains of gonococci and found this to vary between six and 34 hours at 106.7° F.

Sixteen of the 50 patients receiving treatment had arthritis and were uniformly benefited, being listed on discharge as 90 per cent to 95 per cent improved. Eight received one treatment and 8 two treatments. None of these cases were transferred to a hospital for chronic diseases. This was frequently a necessity in the past because of their necessarily long hospitalization.

Two cases of gonorrhea complicated by early pregnancy, have been treated by this method, both requiring 3 treatments. Neither one aborted and one was cured, the other showing a positive urethra but a negative cervix after treatments.

Short wave therapy was substituted for the Elliott treatment in another series of cases in the hope that we could get a still higher pelvic temperature while maintaining the same mouth temperature. Using the short wave machine with a vaginal diathermy applicator at a temperature of 108° F., and the indifferent pad on the abdomen, we did obtain higher rectal readings and should therefore have expected better results.

The patients are just as comfortable with this form of therapy but sweating in the presence of the electric current keeps the nurse on the alert to prevent burns. These burns occur wherever the wires, pad, or vaginal pole touches the patient. In this series we have had three patients who developed pain and swelling on the

inner aspect of the thigh where the wire from the vaginal pole touched them causing a condition resembling a high femoral phlebitis. However, no ill effects resulted, nor did the skin slough.

Vaginal blisters occur with the same frequency as with the Elliott treatment but instead of healing they have a tendency to penetrate to a greater depth. In this small series, two patients developed vesicovaginal fistulas which had to be repaired by surgery. Scar tissue about the opening made these more difficult to repair than the usual fistula of traumatic origin.

In this series of 14 patients, 4 received 1 treatment and 3 were cured and 7 patients received 2 treatments with 5 cures. Three patients were treated with both types of combined methods and 2 were cured. These results are good, but the character and incidence of complications compelled us to abandon the short wave machine.

CONCLUSIONS

1. Hyperpyrexia sustained in the hot box alone at the temperature of 106.7° F. is a very drastic and heroic treatment for the cure of gonorrhea in the female. It requires constant medical supervision in spite of which heat stroke and serious burns may occur.

2. Hyperpyrexia sustained in the hot box in combination with the pelvic short wave therapy, while safe from heat stroke, may produce burns some of which result in the production of vesicovaginal fistulas.

3. Hyperpyrexia sustained in the "hot box" in combination with the Elliott Treatment gives good results without generalized or local dangers. This treatment, therefore, does not require the continual attention of an expert physiotherapist and can be entrusted to a trained nurse. It is adaptable to the average hospital staff. Two treatments with an interval of two days' rest will result in cure in about 84 per cent of cases of acute gonorrhea.

REFERENCES

- (1) *Carpenter and Warren*: New York J. Med. **23**: 997, 1932. (2) *Bishop, F., Lehman, E., and Warren, S.*: J. A. M. A. **104**: 910, 1935. (3) *Desjardins, A., Stuhler, L., and Popp, W.*: J. A. M. A. **104**: 873, 1935. (4) *Bennett, A., and Austin, B.*: Preliminary report of the University of Nebraska Fever Research Project, Reference 5th Annual Fever Conference, pp. 23, 24, May, 1935. (5) *Anderson, T., Arnold, R., and Troutman, J.*: The Treatment of Gonococcal Infections in the Male With Pyreto Therapy, Reference 5th Annual Fever Conference, pp. 33, 34, May, 1935. (6) *Simpson, W., Kislig, F., and Littler, E.*: Ann. Int. Med. **7**: 64, 1933. (7) *Boak, R., Carpenter, C., and Warren, S.*: The Thermal Death Time of 130 Strains of Neisseria Gonorrhoeae, Reference 5th Annual Fever Conference, May, 1935. (8) *Carpenter, C., Boak, R., Mucci, L., and Warren, S.*: J. Lab. & Clin. Med. **18**: 981, 1933. (9) *Warren, S., Carpenter, C., and Boak*: The Basic Principles for the Cure of Gonococcal Infections by a Single Fever Treatment. Reference 5th Annual Fever Conference, pp. 5, 6, May, 1935.

HYPEREMESIS GRAVIDARUM

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IT IS generally stated that approximately one-half of all pregnant women have some degree of nausea and vomiting in the early months of pregnancy. In rare instances the vomiting becomes more frequent and severe.

A study concerning the cases admitted to the University Hospital for hyperemesis gravidarum may be of interest. From June, 1921 to January, 1937, there were 87 patients admitted with this diagnosis. Table I shows that the greatest percentage of cases in the entire group of white and colored occurred between 21 and 25 years of age. This is especially true for the white patients, but it is interesting to note that the greatest percentage of cases among colored patients occurred at an earlier age, probably because these individuals begin their childbearing career younger.

TABLE I. AGE INCIDENCE

	TOTAL	PER CENT	WHITE	PER CENT	COLORED	PER CENT
18-20	16	18.4	10	14.5	6	33.3
21-25	27	31	25	36.2	2	11.1
26-30	16	18.4	11	15.9	5	27.8
31-35	22	25.3	18	26.1	4	2.2
36-40	6	6.9	5	7.2	1	5.6

Table II shows that 95.4 per cent of all the cases occurred in married women and that slightly over one-fourth of the cases occurred among primiparas.

TABLE II. MARITAL STATUS AND GRAVIDITY

	TOTAL	PER CENT	WHITE	PER CENT	COLORED	PER CENT
Married	83	95.4	68	98.6	15	83.3
Single	4	4.6	1	1.4	3	16.7
Primipara	24	27.6	18	26.1	6	33.3
Multipara	63	72.4	51	73.9	12	66.7

Table III refers to the duration of pregnancy on admission to the hospital. It will be seen that the majority of the cases occurred prior to the twelfth week. The correctness of the diagnosis in some of the cases which occurred late in pregnancy may be questioned, as a careful review of the histories points strongly to pyelitis as an etiologic factor in at least two of these.

TABLE III. DURATION OF PREGNANCY

WEEKS	TOTAL	PER CENT	WHITE	PER CENT	COLORED	PER CENT
4-8	18	20.7	13	18.8	5	27.8
8-12	50	57.5	42	60.8	8	44.4
12-16	10	11.5	8	11.6	2	11.1
16-20	1	1.1	1	1.4	0	0
20-40	8	9.2	5	7.2	3	16.7

Table IV on the duration of vomiting prior to hospitalization brings to light many cases in which the vomiting had continued for a considerable length of time before proper treatment was instituted. As a result of this, many patients were admitted in relatively poor condition, showing the effects of starvation.

TABLE IV. DURATION OF VOMITING

WEEKS	TOTAL	PER CENT	WHITE	PER CENT	COLORED	PER CENT
Less than 1	1	1.1	1	1.4	0	0
1-2	10	11.5	6	8.7	4	2.2
2-4	46	52.9	37	55.2	9	50.0
4-8	22	25.3	20	29.0	2	11.1
8-16	8	9.2	5	7.2	3	16.7

Table V shows that more than one-third of the patients suffered from nausea and vomiting in previous pregnancies, and that two patients of the entire series had therapeutic abortions performed for hyperemesis gravidarum in a previous pregnancy. The frequency of syphilis in this group of cases does not show any particular relationship between this disease and hyperemesis. It is clearly demonstrated in the cases under consideration, pregnancy being interrupted 17 times, that any or all of the items just mentioned are by no means incompatible with a continuation of the pregnancy, provided that the patient is properly treated.

TABLE V. ASSOCIATED FINDINGS

	TOTAL	PER CENT	WHITE	PER CENT	COLORED	PER CENT
Nausea and vomiting in previous pregnancies	33	37.9	27	39.1	6	33.3
Therapeutic abortion for vomiting in previous preg.	2	2.3	2	2.9	0	0
Positive Wassermann	4	4.6	1	1.4	3	16.7
Temperature over 99° F.	43	49.4				
Pulse over 100	25	28.7				
Albuminuria	27	31.0				
Acetonuria	59	67.8				
Diabetic acid	41	47.1				

In this series 70 patients were given so-called conservative treatment, consisting of glucose, sedation and complete isolation in addition to a period of from twenty-four to forty-eight hours of starvation. Seventeen of the pregnancies were interrupted or 19.5 per cent of the entire group. Twelve interruptions of pregnancy were done among the white patients, and 5 among the colored; giving an incidence of 17.4 per cent and 27.8 per cent, respectively, for the two races. In addition, Table VI shows that the eye grounds were examined in only 35 cases, all of these being in more recent years since our attention has been called to the significance of eye ground changes in this disease. Hemorrhages in the eye grounds were found in 3 cases, this complication occurring twice among the white patients, and once among the colored. One of these patients was a white primigravida, aged 14 years, who had been vomiting for five weeks prior to admission to the hospital and who at the time of admission was approximately fourteen weeks pregnant. On en-

tering the hospital, her temperature was 100.6° F., pulse rate 140, albumin, acetone and diacetic acid were found in the urine, and hemorrhages were present in both fundi. Her pregnancy was interrupted and she made an uneventful recovery. The other white patient was a thirty-five-year-old multigravida about twenty weeks pregnant who had been vomiting a number of weeks prior to admission to the hospital. Her temperature was 98.6° F., pulse rate 100, with only a slight trace of albumin in the urine. Examination of the eye grounds showed hemorrhages in both fundi, but since this case occurred several years ago the patient was treated conservatively, and showed immediate response to the type of therapy employed and was discharged from the hospital in good condition without an interruption of her pregnancy. The third case occurred in a colored multigravida, aged eighteen years, who was admitted to the hospital in her twelfth week of pregnancy after about six weeks of vomiting at home. On admission, her temperature was 102° F., pulse rate 120, and albumin, acetone, and diacetic acid were present in the urine. She showed hemorrhages and exudate in both fundi. In spite of the interruption of the pregnancy, this patient died. It is quite possible that an earlier interruption of pregnancy might have resulted differently.

TABLE VI. TREATMENT

	TOTAL	PER CENT	PER CENT	WHITE	COLORED	PER CENT
Treated conservatively	70	80.5	59	85.5	11	61.1
Interrupted	17	19.5	12	17.4	5	27.8
Hemorrhages in eye grounds	3	3.4	2	2.9	1	5.6
Eye grounds normal	32	36.8	26	37.7	6	33.3

So far as the results are concerned in this series of patients, 89.7 per cent of the entire group may be classified as good, the frequency of a good result being 92.8 per cent among the white patients and 77.8 per cent among the colored. Four patients, or 4.6 per cent, were discharged from the hospital unimproved. In every instance there was a marked lack of cooperation on the part of the patient, necessitating her discharge from the hospital against the advice of the attending physician. Five patients died, a percentage of 5.6 for the entire series. Two of these were white patients, and 3 colored, giving percentages of 2.9 and 16.7, respectively. Several points are brought out by these figures, such as the often questioned occurrence of so-called neurotic vomiting among colored patients which can be cured without an interruption of the pregnancy. It is also clear, however, that there is a markedly increased mortality

TABLE VII

	TOTAL	PER CENT	WHITE	PER CENT	COLORED	PER CENT
Good	78	89.7	64	92.8	14	77.8
Unimproved	4	4.6	3	4.3	1	5.6
Died	5	5.6	2	2.9	3	16.7
Autopsy	2	40				
Days of hospitalization	1,013	12.8*	706	10.2*	307	17*

*Days per patient.

rate among colored patients suffering from hyperemesis gravidarum. The advisability therefore of treating the condition more radically in colored patients seems to be well borne out. Table VII also shows an average hospital stay of 12.8 days per patient, the figure for the colored patients being considerably higher than that for the white.

SUMMARY

Hyperemesis gravidarum, while a fairly rare complication of pregnancy, does occur with sufficient frequency to create considerable interest. Although the neurotic element cannot be definitely proved, it does seem to play a rather important part in increasing the severity of the symptoms. General rules for treatment are impossible, it being necessary to individualize each case. Many patients will respond to conservative and suggestive therapy. A few require interruption of pregnancy, and in the latter group certain precautions are of the greatest importance.

MATERNAL INTRACRANIAL HEMORRHAGE COMPLICATING LABOR*

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WE WISH to present three cases of maternal intracranial hemorrhage complicating labor observed during the last four years at the Beth Israel Hospital.

Although spontaneous subarachnoid hemorrhage was noted by Bramwell¹ in his classic description of the disease in 1886, its symptomatology has been recognized only in recent years and differentiated from other forms of spontaneous intracranial hemorrhage.

Studies by Eppinger,² Wichern,³ Fearnside,⁴ Hassin,⁵ Symonds,⁶ and Sands⁷ have thrown considerable light on the subject and have established it as a definite clinical entity, one that lends itself to a correct diagnosis.

The occurrence of such hemorrhages in young persons has led many observers to assume that a congenital weakness or defect of the vessel wall leads to the aneurysmal deformity, which later under the strain of hypertension ruptures, causing bleeding.

Fearnside proved that congenital aneurysms must be of not infrequent occurrence, for they were found fifteen times in a series of 5,432 consecutive examinations of the head, one in every 362 cases.

In 1930 Forbes⁸ demonstrated that a number of hitherto unexplained intracranial hemorrhages in young persons can be accounted for on the basis of ruptured intracranial aneurysms of congenital origin in whom there is no evidence of syphilis or atheroma. He found 12 aneurysms in 70 routine necropsies. He called attention to frequent muscular defects in the media of cerebral arteries at the point of their bifurcation, or in the origin of a branch; usually situated on the circle of Willis, or the vessels in its immediate vicinity. This is significant, for it establishes the existence of weak points in a vessel wall, and thus serves as points of predilection for aneurysm. In none of the aneurysms studied in this series can muscle be demonstrated in the wall of the sac.

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Corroboration was given in papers by Schmidt,⁹ Voncken,¹⁰ Chase,¹¹ Tuthill,¹² Strauss,¹³ and Friedman,¹⁴ all of whom reported that spontaneous subarachnoid hemorrhage in young people in the great majority of instances is caused by a ruptured aneurysm of congenital origin.

Schmidt drew attention to the frequent difficulty of finding the aneurysm and emphasized that failure to find an aneurysm does not exclude its existence.

McIver and Wilson,¹⁵ and Stengel and Wolferth¹⁶ believe that mycotic emboli from diseased valves may produce inflammatory lesions of small cerebral blood vessels; and in this way weaken the wall of that vessel through a degenerative process, thus leading to mycotic aneurysm and hemorrhage. In Fearnside's collection of 44 cases of intracranial aneurysms, 13 were due to vegetative endocarditis and septic emboli.

Hypertensive disease or cerebral arteriosclerosis is the most common etiologic factor in aneurysmal formation in patients past middle life, although age does not rule out congenital origin.

Turnbull¹⁷ especially has proved that syphilis is an exceedingly rare cause of intracranial aneurysm; there were none in his and Fearnside's material of 44 cases.

In the absence of generalized disease many patients go through life without ever having symptoms pointing to an intracranial aneurysm, except chronically recurring headache. Bassoe¹⁸ in his treatise on migraine in relation to cerebral vascular lesions reported spontaneous subarachnoid hemorrhage to be relatively frequent in migraine patients. He suggests that the previous migraine-like headache may have been directly due to the congenital aneurysm, and was not true migraine. Goldflam,¹⁹ Adie,²⁰ Critchley and Ferguson,²¹ cite other cases in point, and advocate similar views.

Parker²² believes that the correct diagnosis of a cerebral aneurysm during the life of the patient has been regarded as somewhat difficult. It is only in the cases of cerebral aneurysms with intermittent leakage or rupture that correct diagnosis of the aneurysm is possible. Much more interesting clinically are the cases of intermittent leakage of blood from an aneurysmal sac with alternating episodes of disturbed function and periods of relatively poor health. This phenomenon occurred in 31.1 per cent of Wichern's cases, and in Fearnside's series of 44 cases it was present in about 42 per cent of his nonembolic aneurysms. In these cases there was a history of two, three or more episodes separated by varying intervals.

A thorough search of the literature revealed few published reports, indicating the rarity of recognized cases of spontaneous subarachnoid hemorrhage complicating pregnancy, labor, and the puerperium.

Russel²³ observed the disease in 5 cases, Masten²⁴ in 2 cases, Stroink²⁵ in 2 cases, Ohler²⁶ in 1 case, Strauss in 2 cases, and Smith²⁷ in 1 case. Of these 13 cases reported by the above authors, it is interesting to note that in 8 there was a definite association between this syndrome and toxemia of pregnancy. On the basis of this finding one may have to consider the question of toxemia as a possible cause of subarachnoid hemorrhage, since spontaneous subarachnoid bleeding may result from the bursting of a congenital aneurysm under the strain of hypertension.

Subarachnoid hemorrhage is a striking syndrome with sudden onset of severe headache, vomiting, stupor, or coma, depending upon the size of the rent in the vessels, and slow pulse. Either the patient succumbs immediately to a fulminating hemorrhage; or if she does not, there develops the secondary stage, a meningeal syndrome a few days later. During this stage one finds fever, pain, and rigidity of the neck and positive Kernig sign, and leucocytosis. The most significant of all the findings is the presence of blood in the cerebrospinal fluid under increased pressure. It may vary in color from a pink to a dark red or deep orange. It is intimately mixed with the fluid in the three tubes; it does not clot, and the supernatant fluid on standing is xanthochromic or yellow. In many cases, perhaps the majority, the prodromal symptoms are mild; the initial attack being followed by apparent recovery. Leakage or recurrence of bleeding may occur intermittently. Two to four episodes may occur prior to the final and fatal rupture.

The syndrome of subarachnoid hemorrhage must be differentiated from intracerebral hemorrhage. It differs from the latter by the presence of pronounced meningeal signs, the frequent occurrence of papilledema and paralysis of the extrinsic ocular muscles, and the lack of focal signs.

REPORT OF CASES

CASE 1.—Y. A., para 0, gravida i, aged 25 years, married, presented herself for prenatal care on Aug. 8, 1933, in the fifth month of her pregnancy.

The family history was negative. The patient stated that she had had measles and scarlet fever as a child, but no serious illness or operation.

Her menstrual periods commenced at the age of 17 years and were irregular, occurring every thirty to thirty-five days, and lasting from two to three days. The flow was scant. The last menstrual period was March 23, 1933. The expected date of her confinement was Dec. 30, 1933.

Physical examination revealed a short, well-developed obese woman, weighing 175 pounds. The heart and lungs were normal. Blood pressure was 108/68. Pulse 90. The urine, blood Wassermann, and pelvic measurements were normal. Subsequent antepartum examinations showed the blood pressure to average about 110/60; urinalyses were repeatedly negative. There were no complaints.

Following her last visit to the clinic on October 3, the patient failed to report again for eight weeks. After much persuasion she was induced to return and she presented herself at the clinic on December 12.

There seemed to be nothing unusual about her condition at this time, until she rose from her seat to walk across the room, when she suddenly became dizzy and pitched forward on her face. She did not faint, nor did she lose consciousness. She regained her composure very quickly. The blood pressure was 125/70 and the urine examination was negative. There was no edema of the face, body, or extremities, and no history of headache or visual disturbances. Nor was there any evidence of paralysis of any part of the body. The pupils reacted well. Further questioning at this time revealed the fact that on several occasions during the pregnant state between the period of October 3 and December 12, the patient was subject to frequent attacks of syncope.

Onset of labor occurred at term on Jan. 4, 1933, at 4:30 P.M. The patient was admitted to the hospital on Jan. 5, 1934, at 6:15 A.M., having good uterine contractions at seven-minute intervals. The temperature was 99.2° F., pulse 80, and respirations 20.

The general physical examination on admission was essentially negative. The blood pressure was 140/100. The urine was negative. Rectal examination disclosed the vertex to be engaged above the spines in an R.O.A. position; the cervix was two-plus fingers dilated and thick; the membranes were intact and the fetal heart was in good condition. Pains occurred every five minutes.

The patient had been perfectly well until 11:15 A.M., when she was seized with sudden severe headache and dizziness.

At 11:40 A.M. (twenty-five minutes after the onset of her initial complaint) she was stricken with sudden unconsciousness and coma, became pale and cyanotic, frothed at the mouth and gasped for air. There were no convulsions.

A catheterized specimen of urine obtained at this time was alkaline in reaction; specific gravity 1.018. It contained a trace of albumin, an occasional hyaline and granular cast, occasional white and red blood cells, and epithelial cells. Glucose and acetone absent.

In spite of all that could be done for the patient, she failed to respond and at 11:45 A.M. or exactly five and one-half hours from the time of admission, she died undelivered. The total duration of labor was twelve hours and fifteen minutes.

Necropsy (Dr. A. Plaut).—Gross Observations: The brain appeared relatively small. It weighed 1,215 gm. The outside of the brain except for hyperemia was not very remarkable. The floor of the third ventricle was slightly bulging, and there was a blue sheen directly behind the infundibulum. On the left side of the pons posteriorly there was an irregularly oblong flat hemorrhage 1.5 by 0.4 mm. Indistinct, bloody areas were seen over the cerebellum. The brain was cut frontally

after hardening. All the ventricles were moderately distended. A large intraventricular mass of clotted blood was found tightly filling the fourth ventricle, thus explaining the sudden death. The clot in the third ventricle appeared smaller. The major portion of the pons was occupied by irregular hemorrhage. No tumor and no aneurysm or varix could be discerned with the naked eye. Further slicing of the pontine hemorrhage revealed a still larger hemorrhage, which, in the part of the pons nearest the fourth ventricle, reached a transverse diameter of 3.5 cm. and a vertical one of 3 cm. At this level no brain tissue could be seen throughout the hemorrhage. The hemorrhage also encroached upon the lower leg of the right internal capsule. The region of the corpus of Luys was almost entirely destroyed by the hemorrhage. On a horizontal cut the continuity between the pontine hemorrhage and the clot in the fourth ventricle was seen.

Microscopic Examination: Sections from different areas of the brain did not show any hemorrhage or lesion of blood vessels.

Comment.—The case here reported of intracerebral hemorrhage is of unknown origin. No evidence of hypertensive disease, endocarditis, or congenital aneurysm could be found. The significant findings would indicate that this patient had numerous signs of an abnormal constitution; namely, obesity, late onset of menses, adenoma of hypophysis and abnormal nerve structure in the hypophysis, goiter, and splachnomegaly. This may in a certain measure explain some abnormality in vessel structure which made the so-called spontaneous hemorrhage possible. It certainly is possible that there may have been an aneurysm in the pons which was destroyed by the hemorrhage beyond recognition and therefore escaped notice.

CASE 2.—R. A., para ii, gravida iii, aged 26 years, married, presented herself for prenatal care on Nov. 12, 1935. The family history was unimportant. She had had a renal calculus in her left kidney for which a pyelotomy and nephrotomy was done in March, 1935. The past history revealed the fact that for about three years she had been treated in various clinics for chronically recurring headaches, with no relief. The diagnosis could not be determined. Onset of menses began at 11 years, occurring every twenty-eight days, lasting three days. The last menstrual period was June 25, 1935, and the expected date of delivery was April 1, 1936. She had been delivered spontaneously at term, nine and seven years before. The babies weighed 5 pounds and 5 pounds 13 ounces, respectively. The puerperium was normal. The physical examination was negative. She weighed 125 pounds. The heart and lungs were normal. The blood pressure was 122/62. The urine showed a faint trace of albumin. Blood Wassermann was negative. The pelvic measurements were ample. Subsequent ante-partum examinations showed the blood pressure to range between 110/80 and 100/60. Urinalysis showed a faint trace of albumin. She had gained 21 pounds. Onset of labor occurred at term on March 28, 1936, at 12 noon.

On admission to the hospital at 4:30 P.M. the same day the head was engaged in L.O.A. position, and the cervix was two and one-half fingers dilated. The physical examination was negative. The heart and lungs were normal as were apparently the abdominal viscera. The blood pressure was 130/90. She delivered spontaneously at 6:05 P.M. The weight of the baby was 8 pounds 2 ounces. The total duration of labor was six hours and fifteen minutes. The patient received $\frac{1}{2}$ c.c. of pituitrin following the birth of the baby, and 1 c.c. of ergobasine subsequent to the delivery of the placenta.

At 8:15 P.M., two hours after delivery, the patient vomited and complained of severe headache, dizziness, pain in both eyes, and dimness of vision. There was no loss of consciousness or stupor. The skin was cold and clammy. Both hands were cyanotic up to the wrist. The blood pressure rose to 170/90. The pulse was 64. Ergotism was suspected. A catheterized specimen of urine was acid; specific gravity 1010, with a trace of albumin, no glucose or diacetic acid; microscopically, many red and white blood cells. A chemical examination of the blood showed the non-protein nitrogen to be normal.

The following morning, March 29, the blood pressure dropped to 105 systolic and 70 diastolic and remained constantly at this level. The hands felt warm and appeared entirely normal. A neurologic examination disclosed the following: The patient was in deep stupor but responded promptly and irritably to painful stimuli.

Fundi normal. No cranial nerve palsies. Corneal and palatal reflexes were active and equal. No motor paralysis. Deep reflexes were active and equal. No pathologic reflexes. Abdominal reflexes not obtained due to post-partum abdominal relaxation. She complained of severe occipital and retro-orbital headache when aroused. There was marked rigidity of the neck. Left Kernig sign present. Lumbar puncture yielded uniformly bloody fluid which did not clot. Xanthochromia developed on standing. Her temperature was normal, the pulse 84 and regular, respirations 18, slightly irregular. The diagnosis by Dr. E. D. Friedman was then definitely made as subarachnoid hemorrhage probably due to the rupture of an intracranial aneurysm. Ergot and pituitrin injections may have served as precipitating factors.

On March 30, the second day post partum, the patient still complained of headache, appeared very restless, irritable, somewhat stuporous and disoriented. She had definite nuchal rigidity. Discs were slightly blurred, nasally.

On April 1, the fourth day post partum, the patient appeared more stuporous. The temperature rose to 102.8° F., the pulse ranged between 60 and 70, respirations 24. There was marked cervical rigidity and bilateral Kernig. Lumbar puncture was performed and 15 c.c. of bloody fluid under low pressure was removed. The supernatant fluid was orange colored.

On April 3, the sixth day post partum, her condition remaining about the same for several days, another spinal tap was done, and 15 c.c. of cherry colored fluid was withdrawn.

On April 6, the ninth day post partum, the temperature dropped to a normal level. The pulse was 80. There was a rapid regression of signs. The patient appeared rational and answered questions readily. The reflexes were normal.

Thereafter, the patient made a gradual but uninterrupted recovery and was discharged from the hospital on June 3, 1936, sixty-seven days post partum in apparently good health. The neurologic examination on the day of discharge was completely negative and clear cerebrospinal fluid was obtained. She was requested to report for further observation at regular intervals. When last seen in the Follow-up Clinic on Dec. 21, 1937, she complained of headache and dizziness.

Comment.—This case represents a cerebral aneurysm probably caused by congenital weakness of the vessel wall. The headache of three years' standing may have been due to the presence of the aneurysm acting as a tumor, or possibly, to its intermittent leakage.

The possibility must be kept in mind that ergobasine and pituitrin, the drugs used, may have been but a precipitating cause of leakage from an aneurysm or damaged wall under the strain of hypertension.

CASE 3.—B. K., aged 25 years, para 0, gravida i, appeared for examination on Jan. 22, 1936, at the second month of her pregnancy. The past history was unessential. The patient had enjoyed good health all her life. Menses began at 12 years of age, occurring regularly every thirty days, lasting five days. She last menstruated Nov. 16, 1935. The expected date of confinement was Aug. 13, 1936. The physical examination was negative. The heart and lungs were normal. Height 59 inches. Weight 99½ pounds. Pelvic measurements ample. Blood pressure was 110/80. The urine was normal. Blood Wassermann was negative. Subsequent ante-partum examinations revealed the same findings. Onset of labor occurred at term, on Aug. 19, 1936, at 6 P.M. The patient was admitted to the hospital at 10:35 P.M. The vertex was engaged in L.O.A. position; the cervix was two fingers dilated; the fetal heart heard in the L.L.Q. and in good condition. On Aug. 20, at 4 A.M. examination disclosed the cervix to be fully dilated; the vertex at the spines; the fetal heart in good condition; and pains occurring every three minutes, strong and regular. She delivered spontaneously on August 20, at 7:15 A.M. Medioclateral episiotomy was performed. Weight of baby was 7 pounds 2 ounces. The total duration of labor was thirteen hours and twenty-five minutes. Pituitrin and ergogenin, 1 c.c. each, were given. Light gas and oxygen anesthesia was started.

Approximately ten minutes after delivery of the placenta, and prior to the completion of the episiotomy repair, the patient suddenly became cyanotic, rapidly comatose, respirations ceased; the heart became inaudible, and there was complete disappearance of the pulses simultaneously in both radials. After continuous

artificial respiration including CO₂ and oxygen, intracardiac injection of adrenalin, and the use of the pulmotor, the patient began to breathe, and there was a return of pulsation in the radials. During this time, the patient continued in deep coma and was unconscious. At no time did she have anything resembling a convulsion. The pupils were fixed, dilated, glassy, and did not react to light. There was bilateral loss of corneal sensation. At 12:30 P.M., August 20, the pulse began to lose volume. A continuous intravenous injection of glucose and saline was given, and 300 c.c. of blood by direct transfusion. The patient continued to do poorly and she died at 1:30 P.M. (six hours and fifteen minutes after delivery).

Permission for an autopsy could not be obtained.

On lumbar puncture post mortem, the cerebrospinal fluid was uniformly pink in all three tubes. There was no clotting of the blood and when it had settled the supernatant fluid remained quite yellow. Microscopically, the spinal fluid contained 6,880 R.B.C. per c.mm. A cisternal puncture corroborated the above findings.

Comment.—Whereas the most conclusive evidence of subarachnoid hemorrhage is afforded by the state of the cerebrospinal fluid, this did not aid us in distinguishing the source of the hemorrhage, whether it was of primary meningeal origin or whether it came from an intracerebral hemorrhage which had broken through into the subarachnoid space. Accurate differential diagnosis in comatose patients between cerebral hemorrhage and subarachnoid hemorrhage is difficult. The foregoing case presented several features characteristic of intracranial aneurysm with rupture. 1. The patient was relatively young (25 years of age). 2. The blood pressures were low, varying from 108 systolic and 80 diastolic to 116 systolic and 80 diastolic. 3. There was no evidence of clinically discoverable disease such as arteriosclerosis, local or general infection or endocarditis. It is in cases of this sort that one expects to find rupture of a congenital aneurysm if autopsy is performed.

SUMMARY AND CONCLUSIONS

1. Three cases of maternal intracranial hemorrhage complicating labor have been described. Death occurred as a result of this hemorrhage in two cases. In one the autopsy revealed a large pontine hemorrhage; in the other, the post mortem was not done, but lumbar and cisternal punctures showed the presence of blood in the subarachnoid space. The remaining patient is still alive.

2. Subarachnoid hemorrhage may be due to congenital defect or weakness of the vessels, mycotic aneurysmal disease of the cerebral vessels, and hypertensive disease.

3. Spontaneous subarachnoid hemorrhage is most frequent in young persons suddenly stricken while in apparent perfect health. Congenital aneurysm undoubtedly is the underlying factor in the majority of cases. Leakage of blood into the subarachnoid space at the base of the brain gives rise to clinical signs upon which the diagnosis of this occurrence may be made with reasonable certainty. The presence of blood in the cerebrospinal fluid aids in confirming the diagnosis.

4. No history of toxemia or hypertensive disease could be obtained in our group; contrary to the cases reported in literature where there was a definite association between this syndrome and toxemia of pregnancy.

5. We found no causal relationship of ruptured intracranial aneurysm to pregnancy itself except so far as this pregnancy might have tended to elevate the blood pressure either by the strain of labor or the use of oxytocic drugs. Therefore oxytocics should be avoided during labor in patients suspected of intracranial aneurysm. These drugs prob-

ably serve as precipitating factors (Case 2). The routine administration simultaneously of two oxytocic drugs, such as pituitrin and gynergen in doses of 1 c.c. each, following the third stage of labor should be avoided. Their indiscriminate use may lead to rupture of a congenital intracranial aneurysm even though this condition is not suspected (Case 3).

6. Patients who give a history of persistent or chronically recurring headache, or other prodromata prior to or during pregnancy and labor, when there are no signs of clinically discoverable disease, require the strictest watchfulness by those attending the case. It is advisable to make an ophthalmoscopic examination whenever a patient complains of headache. A complete neurologic examination will do away with many of the diagnostic errors. Incidentally this was not sufficiently stressed in two of the cases.

7. If the diagnosis of aneurysm can be made, it may be advisable to spare the patient the hazard of labor by cesarean section, in the hope that this may ameliorate the mother's condition, inasmuch as repeated leakage or recurrence of hemorrhage under stress usually occurs with these lesions.

8. The patients who recover should be periodically examined and cautioned against exertion of any nature.

9. A study of the literature shows that cases of spontaneous subarachnoid hemorrhage are frequently encountered in neurologic wards. The infrequency of subarachnoid hemorrhage complicating labor is established so far as published reports are concerned. It is our belief that it occurs more frequently than is generally appreciated. The failure to report intracranial aneurysms oftener may be due to the fact that they are being overlooked.

REFERENCES

- (1) *Bramwell, B.*: Edinburgh M. J. 32: 101, 1886. (2) *Eppinger, H.*: Arch. f. Klin. Chirug. 35: Supplem. S.I., 1887. (3) *Wichern, H.*: Deutsche Ztschr. f. Nervenheilk., Leipzig 44: 220, 1912. (4) *Fearnside, E. G.*: Brain 39: 224, 1916. (5) *Hassin, G. B.*: Arch. Neurol. & Psychiat. 17: 770, 1927. (6) *Symonds, C. P.*: Guy's Hospital Reports 73: 139, 1923; Proc. Roy. Soc. Med. 17: 93, 1924; Quarterly J. Med. 18: 93, 1924. (7) *Sands, I. T.*: Arch. Neurol. & Psychiat. 21: 30, 1929. (8) *Forbes, W. D.*: Bull. Johns Hopkins Hosp. 47: 239, 1930. (9) *Schmidt, M.*: Brain 53: 489, 1930. (10) *Voncken, J.*: Frankfurt. Ztschr. f. Path. 42: 41, 1931. (11) *Chase, W. H.*: J. Path. & Bact. 35: 19, 1932. (12) *Tuthill, C. R.*: Arch. Path. 16: 630, 1932. (13) *Strauss, I., and Tarachow, S.*: Arch. Neurol. & Psychiat. 38: 1937. (14) *Friedman, E. D.*: Cecil: A Text Book of Medicine, ed. 4, Philadelphia, 1937, W. B. Saunders Co., pp. 1413. (15) *Melver, J., and Wilson, G.*: J. A. M. A. 93: 89, 1929. (16) *Stengel, A. E., and Wolferth, C. C.*: Arch. Int. Med. 37: 527, 1923. (17) *Turnbull, H. M.*: Brain 41: 50, 1918. (18) *Bassoe, P.*: J. A. M. A. 101: 599, 1933. (19) *Goldflam, S.*: Deutsche Ztschr. f. Nervenheilk. 76: 158, 1923. (20) *Adie, W. J.*: Lancet 2: 237, 1930. (21) *Critchley, M., and Ferguson, F. R.*: Lancet 1: 123 and 182, 1933. (22) *Parker, H. L.*: Arch. Neurol. & Psychiat. 16: 74, 1926. (23) *Russel, C. K.*: Canad. M. A. J. 28: 133, 1933. (24) *Masten, M. G.*: Wisconsin M. J. 34: 168, 1935. (25) *Stroink, J. A.*: Nederl. tijdschr. verosk. en Gynaec. 39: 240, 1936. (26) *Ohler, W. R., and Hurwitz, D.*: J. A. M. A. 98: 1856, 1932. (27) *Smith, S.*: Nederl. tijdschr. v. geneesk. 772: 3855, 1933.

DISCUSSION

DR. EMANUEL D. FRIEDMAN.—Dr. Moskowitz has called attention to a symptom complex which is not at all unusual in neurologic wards. I think it was well worth while for him to have brought this subject before the obstetrician because for a long time even the medical man was not conversant with this syndrome. Many a house officer was blamed for being unskilled in obtaining spinal fluid because he got a "bloody tap" and frequently he was called to task for disturbing the general management of a case, by the introduction of this extraneous factor; but it soon became evident to most of us that these "bloody taps" were not all due to hemorrhage at the time of puncture. As Dr. Moskowitz said, the type of fluid obtained in these cases is quite different from that which one gets in cases of simple trauma from tapping of the vein at the time of puncture. In the latter instance, the first tube of fluid will be bloody and the subsequent tubes become more and more clear, whereas in true subarachnoid hemorrhage all the tubes are uniformly bloody. If one allows the fluid to stand in the tube, in cases of traumatic admixture of blood, one sees the formation of a clot, while in cases of subarachnoid bleeding there is no clot formation. The reason for this is that the rent which takes place in the aneurysmal sac is quickly covered by fibrin deposit, and then all that happens is a seepage of red blood cells into the spinal fluid, *without fibrin*, so that one has characteristic fluid, which is full of blood and yet contains no fibrin and, therefore, does not clot. If one allows the fluid to stand, one gets various types of discoloration in the supernatant fluid to which Dr. Moskowitz referred. Today most house officers recognize when they are dealing with a case of traumatic admixture of blood and when they are dealing with a case of true subarachnoid bleeding.

As Dr. Moskowitz has well said, syphilis seldom plays a role in these cases. In our experience, which has been fairly large, I know of only two or three instances in which we obtained a positive Wassermann in the blood, and they were all in colored patients.

As a rule, the etiologic factors concerned are those given by Dr. Moskowitz, namely, hypertensive disease and mycotic aneurysmal disease of the cerebral vessels and, finally, there is the group of young people who suffer from so-called congenital aneurysms. These are the cases that used to come to the post-mortem table of the late Dr. Charles Norris, Chief Medical Examiner of New York City, young persons suddenly stricken while in apparent perfect health with coma immediately supervening and rapid death. If the base of the brain is examined in such cases, one finds a sac which takes origin from one of the blood vessels forming the circle of Willis. In some instances, the medical examiner cannot be sure, but suspects that he is dealing with such an eventuality.

When the aneurysm has ruptured, the diagnosis is fairly simple. Most of us recognize this entity. The patient develops headache, vomits and goes into stupor or coma, depending upon the size of the rent in the vessels, the pulse becomes slow, and the individual exhibits no focal signs such as one sees in intracerebral bleeding. After a few days, if the hemorrhage does not terminate fatally, there develops the secondary stage, a meningeal syndrome, which is a reaction to the presence of blood in the subarachnoid space. It is really a foreign body meningitis. If the case is seen during this stage, one finds fever, leucocytosis, stiff neck and a positive Kernig, and one is led to think he is dealing with a case of infectious meningitis until he puts a needle in and obtains the characteristic fluid. As a rule, the patients who do not succumb immediately to a fulminating hemorrhage get well, and after ten or twelve days leave the hospital; as Dr. Moskowitz said, they may go through three or four episodes of such subarachnoid bleeding and experience no more episodes.

In the case of rupture, the diagnosis, as I have already stated, is not difficult; but prior to rupture it is somewhat more difficult to make the diagnosis. There are, however, a few symptoms and signs which may lead one to suspect the presence of an intracranial aneurysm. These are oculomotor paralysis involving the third or sixth nerve, a certain amount of trigeminal pain in the distribution, particularly of the upper branch of the fifth nerve, some disturbance of the sense of smell on the affected side, and possibly interference with vision on that side.

I had the privilege of observing a case of intracranial aneurysm in which the diagnosis had been made *intra vitam* and the subsequent course of events proved the diagnosis to be correct.

If one finds a hemianopsia in such a case, it is additional evidence of the presence of a possible aneurysm, but many of these patients, as Dr. Moskowitz has said, go through life without ever having symptoms pointing to an intracranial lesion, except perhaps chronically-recurring headache.

In the first case reported by Moskowitz the periodic attacks of syncope antedating the final insult seemed to point to a constitutional dyscrasia, possibly similar to what Osler called poor tubing, a vascular dyscrasia in the patient which ended in hemorrhage into the pons. These aneurysms usually do not occur in the substance of the brain stem or the brain, but commonly take their origin from one of the branches that go to make up the circle of Willis, and are usually at the base.

In the second case the diagnosis was clear, the patient ran a typical course and recovered.

In the third case also I believe the diagnosis was justified. This type of case is similar to the ones which come to the medical examiner's office. In these cases it is necessary to make a diagnosis between intracerebral bleeding and rupture of an aneurysm. In this connection, if there are pronounced meningeal signs, the likelihood of rupture of an intracranial aneurysm is greater than if there are no meningeal signs.

Parenthetically, may I say that the abolition of the corneal reflex in cases of stupor is of considerable diagnostic significance. This reflex is usually abolished on the side of the hemiplegia. In the absence of other clear evidence of a cerebral vascular accident, I have found this sign very helpful. It is particularly useful in the so-called acute cases that come to the hospital with the diagnosis of either acute alcoholism or some other form of intoxication.

In closing, I think it was well worth while for Dr. Moskowitz to have brought this symptom complex before this group, and I agree with his conclusions, except that one would have to repeat what he said and what I have already hinted at, namely, that a diagnosis of intracranial aneurysm prior to rupture is exceedingly difficult unless it takes origin from the internal carotid or one of the branches of this vessel and gives rise to trigeminal pain and the ocular palsies to which I have referred.

Schultze-Rhonhof: On the Treatment of Pruritus Vulvae, Zentralbl. f. Gynäk. 61: 610, 1937.

The actual cause of this condition is not definitely established, and for this reason many methods of treatment have been adopted with varying results.

The author for many years had a patient, now 73 years old, under his care who suffered from most intractable pruritus. Anesthetic ointments, balsams, powders, painting with silver nitrate solutions, resorcin pastes and sitz baths of various kinds, vitamin A and ovarian preparations, and x-ray therapy were all equally ineffective.

Finally, in desperation, the author instructed the patient to coat the vulva with fresh honey. Improvement was obvious within a few days and continuation of the nightly application over a period of some weeks was followed by disappearance of the intense itching which did not recur even after the treatment was discontinued.

Since then the author has tried this therapy for numerous cases of pruritus with the same satisfactory result. He feels unable to give any satisfactory explanation for the efficacy of honey.

J. P. GREENHILL.

KRUKENBERG TUMOR COMPLICATING PREGNANCY*

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UP TO the present time, some 90-odd cases of Krukenberg tumor have been reported in the literature. None of them, so far as I can ascertain, showed pregnancy as an associated condition, or complicating factor. For this reason I wish to report the following case:

Mrs. N. K., white, aged 33 years, para iii, was admitted to the First Obstetrical Service, Methodist-Episcopal Hospital, on Nov. 23, 1935, acutely ill, complaining of vomiting, weakness, and loss of weight for the past three weeks.

Her last menstrual period occurred June 16, placing her approximately in the fifth month of gestation. There was no history of hyperemesis or other toxic symptoms with the previous pregnancies, and delivery and puerperium were uneventful. The menses were always normal, her family and past history irrelevant. She had always considered herself a healthy individual. In the middle of October, 1935, about 5 weeks before the onset of the present illness, the patient had noted a painless lump in the left breast, with a subsequent black discharge from the nipple. A short time thereafter a mass appeared in the right breast. Both masses had steadily grown larger during pregnancy.

The first trimester of this pregnancy had been uneventful, and the onset of her present illness began about November 2, three weeks prior to admission. She then became nauseated, began to vomit, and was unable to retain any solid foods or liquids. There was a rapid loss of weight, and she felt weak.

* On November 9, one week after onset, she was admitted to King's County Hospital with a diagnosis of toxemia of pregnancy. X-ray of the abdomen on November 19 showed evidence of one fetus and a questionable second. It was also felt that hydramnion was present, because of excessive size of abdomen for the time of pregnancy. At her own request, but against advice, she was discharged somewhat improved, November 20, eleven days after entering the institution.

Because of continuous vomiting, anorexia, and loss of weight, she was admitted to the Obstetrical Service of the Methodist-Episcopal Hospital, November 23.

Physical examination on that day revealed a seriously ill, pale, emaciated woman appearing much older than the stated 33 years. Lips and mouth were dry, tongue coated, teeth markedly carious, and there was a strong acetone odor to the breath. The breasts were rather small, and in each was found a hard, somewhat irregular, nontender, freely movable mass. The right measuring about 6 by 8 cm., and the left 4 by 7 cm. There was no discharge from either nipple. Both axillae presented several almond-sized nodes. The lungs were clear and the heart negative except for tachycardia.

Relaxation of the abdominal walls was marked, with considerable diathesis of the recti muscles. Her abdomen which was enlarged to the size of a seven months' pregnancy, revealed two indistinct masses, apparently arising from the pelvis. They were rather irregular in outline, and the one on the left side was larger than that on the right. A definite fluid wave could be felt. No fetal heart was heard.

Pelvic examination showed a relaxed vaginal wall, bilaterally lacerated and eroded cervix. The uterus could not be clearly defined from the two masses, but it was thought she was 5 to 6 months' pregnant. Reflexes were normal and there was no edema of the extremities. Temperature on admission was 98.6° F., pulse 90,

*Presented at the Annual Meeting of The Associated Physicians of Long Island, January, 1936.

respirations 20. Urinalysis showed faint trace of albumin, 4-plus acetone, 2-plus diacetic acid, many granular casts. The R.B.C. numbered 2,950,000, the W.B.C. 18,600, and Hg 55 per cent. Sedimentation time was fifty-five minutes. The blood chemistry was normal, and the Wassermann negative.

Clinical Diagnosis.—Pregnancy, with possible twins, toxemia, pelvoabdominal tumor, ascites, carcinoma of both breasts.

She reacted well the first day to 10 per cent glucose by vein, 5 per cent glucose by rectum, clyses, and nothing by mouth. When, however, fluids and frequent small feedings were begun twelve hours after admission, vomiting recurred. Hyperemesis continued despite treatment. Because of her desperate state, it was decided to terminate pregnancy, and on the afternoon of November 25, the membranes were ruptured, and a No. 3 Voorhees bag was inserted into the cervix. Following induction her condition became progressively worse, and she died six hours later.

Postmortem Examination.—The autopsy performed by Dr. E. B. Smith, showed in part the following interesting conditions: Each breast contained a large, asym-

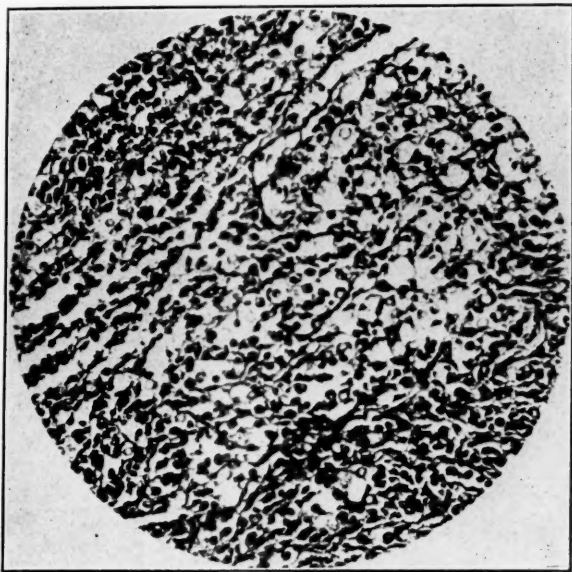


Fig. 1.—Photomicrograph of section of right ovary.

metrical, solitary tumor. The one in the right breast was 15 cm. in diameter, that in the left 10 cm. The tumors were circumscribed, but not encapsulated, and occupied all of both breasts. On section they were hard, white, and lobular.

Upon opening the peritoneal cavity, about 2,000 c.c. of brown fluid escaped. The mid-abdomen was filled with a large tumor which sprang from the left ovary. The stomach was normal in size and contained dark brown fluid. There was a tumor on the posterior wall 4.5 cm. from the pylorus. The growth was 8 cm. long, 4.5 cm. wide, and 0.5 cm. thick, and the edge was sharply outlined. The surface was smooth, white, and homogeneous. Near the pyloric end of the tumor was a crater 1 cm. in diameter and 7 to 8 mm. deep. The edge was sharply punched out, the sides were sloping, and the floor was covered with a yellow substance. In appearance it resembled a peptic ulcer. The remainder of the stomach presented normal rugae, and the mucosa was smooth and pale. There was a string of enlarged nodes along the greater curvature. On section these were firm, white, and homogeneous. The pancreas was of normal size and showed a gray, lobular structure. The

uterus was 18 cm. long and contained a five months' fetus. The left ovary was replaced by a large tumor, weighing 4,200 gm., and measured 26 by 20 by 16 cm. It was divided into several large lobes, and was enclosed in a fibrous membrane. On

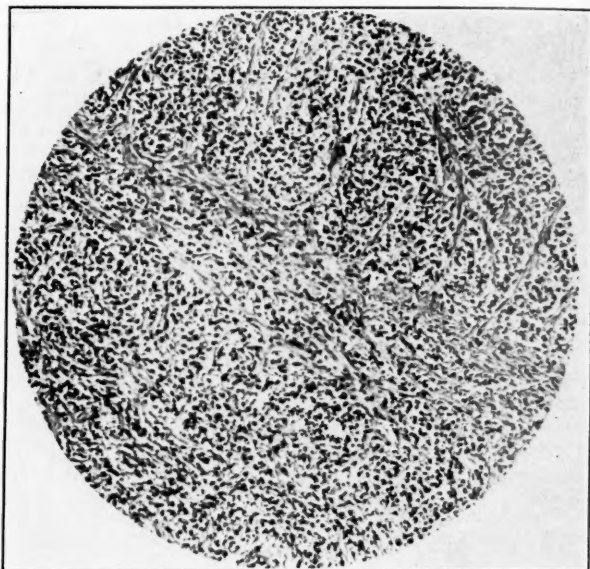


Fig. 2.—Photomicrograph of section of stomach.

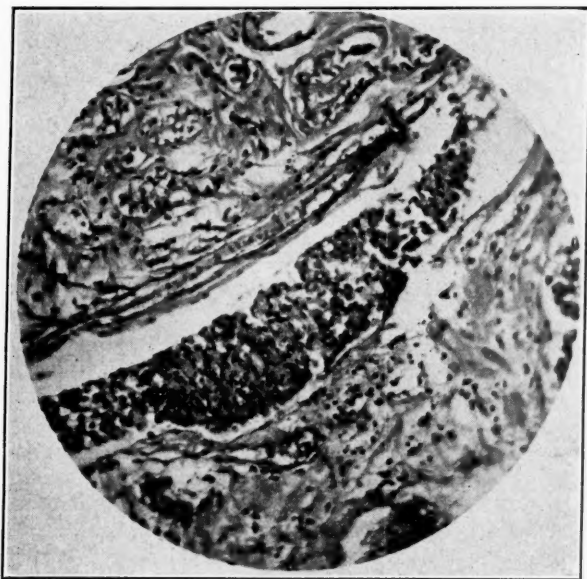


Fig. 3.—Photomicrograph of section of right breast.

section it was solid throughout. In some areas the cut surface was dark red, homogeneous and hemorrhagic, while in others it was mottled gray and yellow, and the tissue was soft, friable, and apparently necrotic. The right ovary was somewhat

enlarged, but the normal contour was well preserved. It measured 4.5 by 3.5 by 2 cm. On section most of the ovarian tissue was replaced by a white, uniform growth. The tubes appeared normal.

Microscopic Examination.—*Stomach:* In the ulcerated area the mucosa was replaced by a new growth, most of which had sloughed away, leaving a narrow rim of partly necrotic tumor tissue lying above the muscularis mucosae. The growth was composed of epithelial cells of variable size and shape, with granular acidophile cytoplasm, and dark oval nuclei. At the edge of the tumor the mucosa was replaced by diffuse carcinoma, supported by a delicate stroma. The cells were large, polyhedral with opaque, acidophile cytoplasm and eccentric nuclei. A few of the latter were crescent shape. Many of the cells were degenerated. Groups of tumor cells were also found in the muscularis. *Right Ovary:* The sections showed small groups of tumor cells enclosed in a network of delicate fibrous tissue. The cells were round or oval, enlarged, pale, with crescentic nuclei pushed to the edge of the cell, forming typical signet ring cells. *Left Ovary:* All of the sections showed the same kind of cells as in the stomach and right ovary. *Breasts:* The gland tissue in both was proliferating, and the picture was approaching that seen in the lactating breast. The stroma was infiltrated with groups of tumor cells, like those previously described. In the Fallopian tubes some of the lymphatics in the wall were filled with tumor cells resembling those found elsewhere.

Pathologic Diagnosis.—Diffuse ulcerative carcinoma of the stomach, bilateral secondary Krukenberg tumor of the ovaries, bilateral secondary Krukenberg tumor of the breasts, with metastases in the Fallopian tubes and pancreas.

Was the primary tumor in the stomach or ovary? Histologic examination points to a gastric origin. Most recent writers feel that Krukenberg tumors are usually secondary to carcinoma of the stomach or intestines. Ewing believes that "the pure Krukenberg tumor is always secondary." However, proof as to origin, structure, and manner of transmission are still lacking.

Summary.—The case here reported shows characteristic Krukenberg tumors of both ovaries and breasts, with involvement of other organs, and a probable primary focus in the stomach. It is especially interesting because of the brief duration and paucity of symptoms, and its association with pregnancy.

THE PATHOLOGIC PROPERTIES OF MECONIUM*

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THE general textbooks on obstetrics and pediatrics contain scant reference to meconium beyond the fact that it is the first excreta of the newborn, and perhaps enumerate the various constituents of meconium (Williams¹). The clinical literature, on the other hand, has a considerable number of papers which deal with the various physical and chemical properties of meconium (Sheldon and Ramage, Passini, Norton and Shohl, Giaume and Lanza), and more particularly with its pathologic manifestations as is occasionally seen in cases of meconium ileus or peritonitis in the newborn.

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According to Gierke meconium peritonitis may be applied to those cases in which there is demonstrable within the peritoneum meconium, calcified meconium, mucous droplets, foreign body giant cells, cells from the source of perforation, fibrinous or fibrous adhesions, and rarely, lanugo hair. Boikan, Kornblith and Otani, and Dodd report cases of meconium ileus and in their papers review extensively the literature on the subject. Snyder, and Hall have studied the bacterial flora of the first specimens of stools of newborns and Snyder has done the same for meconium from stillbirths.

The senior author has been impressed by the observation that in cases of cesarean section meconium contamination of the spill into the peritoneal cavity or into the operative incision of the mother may lead to a peritonitis of varying degrees of severity, or to a delayed healing of the abdominal wound and a stormy convalescence. It is rather strange in view of the complete literature on the subject of meconium, that no one has thought of conducting experiments dealing with the pathologic and biologic properties of this material. The present communication is a report of investigations along these lines.

METHODS

The meconium used in these experiments was obtained on the maternity floor of Michael Reese Hospital from newborn infants at the time of delivery and was collected under sterile precautions. The scope of the work may be divided as follows:

1. *Toxicity experiments:* Minimal lethal dose in rats and the effect of a filtered solution of meconium when injected intravenously upon the blood pressure and respiration of anesthetized dogs.
2. Effects of meconium administered intraperitoneally, intramuscularly, and subcutaneously to rats and dogs.
3. Effects of instillation of unfiltered meconium into the uterus of dogs.
4. *Bile controls:* Since biliary tract products are among the chief constituents of meconium, it was deemed advisable to repeat certain of above experiments using bile instead of meconium. The bile used was sterile upon culture and was procured from fresh human autopsy material.

RESULTS

Toxicity Experiments.—Five rats were injected intraperitoneally with varying amounts of sterile undiluted meconium (from $\frac{1}{4}$ to 1.5 c.c.) by means of a syringe and an 18 gauge needle. Objectively the rats were well and at autopsy three days later the abdominal cavities of the rats showed the following changes: the omenta were somewhat discolored, the abdominal cavities contained a small amount of fluid and bits of inspissated meconium clung to and stained some of the intestinal coils.

In two dogs under nembutal anesthesia, it was observed that small amounts of a filtered suspension of meconium in saline solution injected intravenously caused a marked and prolonged depression of blood pressure and an increase in amplitude and frequency of respiration as is seen after the injection of bile; a somewhat larger dose was fatal, the dogs not recovering from the effect and dying from heart failure.

Effects of Intraperitoneal, Intramuscular, and Subcutaneous Injection.—Three grams of meconium were thoroughly mixed in 15 c.c. of sterile saline and 5 c.c. of the mixture injected intraperitoneally into each of three female rats. One week later the rats were normal to outward appearances and were autopsied. The abdominal cavities contained a slight amount of murky fluid and the omenta had a dirty yellowish discoloration and also seemed somewhat contracted and matted together. Microscopic examination of the omentum revealed areas of myxomatous

connective tissues containing masses of polymorphonuclear leucocytes; occasional round cells were seen. The nuclei of the connective tissue elements varied considerably in chromatin content, frequently containing nucleoli and mitotic figures. Diagnosis: marked proliferation of connective tissue, apparently in response to a chronic inflammation, and early scar tissue formation.

A young 20 pound male dog was injected intraperitoneally with 20 c.c. of a thick suspension of meconium in saline; the dog showed no untoward effects and was killed and posted on the fifth day following injection. *The gross findings:* the peritoneal surfaces were smooth and shiny but the abdominal cavity contained about 60 c.c. of a somewhat turbid dirty yellow fluid; the omentum was hyperemic and somewhat reddish brown in color; spleen slightly enlarged and moderately firm; the upper surface of the right lobe of the liver contained a bit of inspissated meconium and was adherent to the diaphragm by soft adhesion. Microscopic examination revealed moderate hyperplasia of the spleen, and swelling and degeneration of the tubular elements of the kidney. The area of diaphragm adherent to the liver contained a fibrinous exudate upon its serous surface and enmeshed in the fibrinous network were scattered clumps of both round cells and polymorphonuclear leucocytes.

Intramuscular Injection.—One cubic centimeter of an unfiltered boiled 10 per cent suspension of meconium was injected into the right thigh of a rat. The animal developed a palpable abscess and was killed two weeks later. An abscess measuring about 1 by 1 by 1 cm. was situated in the muscles of the medial aspects of the thigh; the abscess contained a thick brownish yellow material very much like an admixture of pus and meconium. Histologically the abscessed area contained many round cells and degenerated muscle fibers and nuclei; a wall of leucocytes and connective tissue cells surrounded the area of necrosis, and even beyond the walling-off process muscle fiber showed degeneration.

Subcutaneous Injection.—One cubic centimeter of the above suspension was injected into the flank of another rat, and it too was killed two weeks later. At autopsy the animal had a subcutaneous abscess which also extended into the deeper tissues. The area measured 2 by 2 cm., appeared grayish yellow in color, and resembled a localized cellulitis. *Pathologic diagnosis:* chronic organizing inflammatory reaction with prevalence of round cells; infiltration of adjoining muscle tissue by round cells and disintegration of muscle fiber.

Instillation of Unfiltered Meconium Into the Uterus.—After performing laparotomy, the uteri of two dogs were incised (about one inch) and the right uterine horn in each case was soiled with several bits of sterile meconium. The uterine incisions were then closed in the usual way and the animals killed on the fifth and tenth days, respectively, following the operation. The autopsy findings are essentially the same for both animals; the right horn is encased by soft adhesions, the serosal surface in the region of the incision is markedly injected and enlarged in comparison with the left horn. Upon opening the uterus, the lumen was filled with a thick brownish material and grossly the mucosal surfaces of both horns seemed similar. Microscopically, the infected horn showed evidences of an acute inflammatory reaction, viz., fibrinous plaques with clumps of leucocytes, edema and round cell invasion of the superficial layers of the endometrium.

Bile Controls.—Toxicity experiments. A series of rats were injected intraperitoneally with graded amounts of sterile human bile ($\frac{1}{2}$ to 2 c.c.). The rats seemed normal and were killed at intervals of from three to ten days after injection. A typical protocol: the peritoneum was shiny, but the blood vessels were prominent; the abdomen contained a small amount of clear fluid and several of the intestinal coils were bile tinged; soft adhesions of omentum to liver. *Microscopic examination:* A number of round cells were present in the omentum and several areas of hyaline-like material were found. The spleen was hyperemic and somewhat hyperplastic.

Intramuscular Injection.—Each of two rats received 0.5 c.c. of bile into the thigh muscles of the right hind leg; the rats were killed, seven and eight days following injection; the one killed on the seventh day had gross enlargement and indura-

tion of the thigh to palpation, the tissues were bile stained, and upon exposing the abscess it was seen to be a firm nodule the size of a pea, the center of which was necrotic tissue. The animal which was sacrificed on the eighth day showed nothing grossly beyond yellowish discoloration at the area of injection, but upon microscopic examination localized areas of granulation tissue were seen; the connective and areolar tissue contained many lymphoid elements and a small lymph node present was definitely hyperplastic.

Subcutaneous Injection.—Each of two rats was injected with 0.5 c.c. of bile subcutaneously in the right flank. At autopsy one week later the sites of injection revealed naught beyond discoloration by the bile, and histologic examination was essentially the same in both, to wit: diffuse round cell infiltration, edema, hyalinization, and areas of hyperemia and extravasation of blood.

DISCUSSION AND CONCLUSIONS

It should be emphasized first that all samples of meconium used in experiments were sterile to bacteriologic culture and any effects observed are due to the substance under investigation and not due to bacterial contaminants. A review of the protocols shows that meconium possesses definite toxic properties of a low grade nature, very similar to those of bile, but much more pronounced in its local effects than bile. This perhaps is due to certain of the constituents of meconium such as lipoids, lanugo hair, epithelial debris, etc., which lend to it its viscid gelatinous consistency, and explain more intense, irritating local action, viz.: Intramuscular and subcutaneous abscesses are much more marked and localized in case of meconium than in case of bile. It has been seen that intraperitoneal injection of meconium into rats is invariably followed by definite pathologic sequelae, such as omental reaction, serous exudation, etc., and at the same time one must keep in mind the fact that rats are notoriously resistant to the ordinary human infections. Bile is very toxic when administered intravenously and a filtered meconium suspension possesses the same property to a lesser degree, since the latter contains less of the bile salts than does pure liver or gall bladder bile. An important fact is, that meconium may produce adhesions in places where it is carried by peristalsis (see experiments on dogs).

The principal practical value of this work concerns its application to the technique of cesarean section. Adequate protection of viscera and peritoneal surfaces is omitted by many operators and suction apparatus may be inadequate or unobtainable. Fortunately, contamination with meconium is not frequent and when meconium escapes in semisolid form, it may easily be wiped away, but when a considerable amount of amniotic fluid with much meconium in suspension gushes into the field of operation, the tissues become bathed in the mixture. The occasional case demanding cesarean section when intrapartum infection exists should be especially safeguarded since meconium encourages adhesions in general as well as infection and suppuration in the operative field. When a large amount of amniotic fluid is demonstrable, vaginal rupture of the membranes may be done in order to forestall any possibility of spill of the liquid contents into the peritoneal cavity.

SUMMARY

1. Meconium possesses a low grade toxicity and resembles bile in its pathologic properties, but produces a greater local inflammatory reaction than bile.

2. Our findings confirm and show a definite basis for the observation that the spill containing meconium escaping into the peritoneal cavity of the mother or into the operative incision may lead to a peritonitis, to adhesions, or to delayed healing of the uterine and abdominal wound.

3. This work emphasizes the necessity of adequate protection of all surfaces in the operative field from the contents of the amniotic sac when performing an abdominal cesarean section.

We are indebted to Dr. M. Corrigan for the histological studies and to Dr. H. Necheles, Director of G. I. Research, for advice and facilities offered.

REFERENCES

- (1) *Williams, J. W.*: Obstetrics, New York, D. Appleton Century Company, p. 422. (2) *Sheldon, J. H., and Ramage, H.*: Biochem. J. 27: 674, 1933. (3) *Passini, F.*: Ztschr. f. Kinderh. 53: 175, 1932. (4) *Norton, R. C., and Shohl, A. T.*: Am. J. Dis. Child. 32: 183, 1926. (5) *Giaume, C., and Lanza, P.*: Pediatra 37: 519, 1929. (6) *Boikan, W. S.*: Arch. Path. 9: 1164, 1930. (7) *Kornblith, B. A., and Otani, S.*: Am. J. Path. 5: 249, 1929. (8) *Dodd, K.*: J. Pediat. 9: 486, 1936. (9) *Snyder, M. L.*: Ibid. 9: 624, 1936. (10) *Hall, I. C., and O'Toole, E.*: Am. J. Dis. Child. 47: 1279, 1934. (11) *Snyder, M. L.*: J. Pediat. 9: 633, 1936.

SEPSIS PUERPERALIS THROMBOPHLEBITICA PUTRIDA (SCHOTTMÜLLER SYNDROME)

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MANY investigators have, from time to time, noted and reported the presence of anaerobic streptococci, in the genital tract of normal pregnancies as well as in the uteri and blood stream in cases of postabortal and puerperal sepsis. Krönig, in 1895, demonstrated obligate anaerobic streptococci in the female genital tract, work that was corroborated by Menge and later by Stöhler and Winkler, who found anaerobic bacteria, for the greater part streptococci, in uterine cultures, in one-third of all their normal, fever-free post partums. Böhne was able to show the presence of anaerobic streptococci in the vaginal secretion of 20 per cent of his ante partum cases; these observations were confirmed by Natwig and Wegelius who found an even greater incidence. In America, Williams in 1898, Wadsworth and A. W. Lea, independently, confirmed the work hitherto reported.

It remained, however, for Schottmüller to arouse the curiosity of the obstetrician and gynecologist to more than mere academic interest in the detection and culture of this group of cocci, to observe the clinical picture produced by these bacteria, and to culture anaerobically all cases of postabortal and puerperal infection and thereby prove that hitherto negative aerobic cultures were very frequently positive when grown anaerobically.

Schottmüller's syndrome is characterized by: foul lochia (produced by putrid endometritis), high intermittent temperature, chills, many small or one large lung abscess (resulting from embolism), pneumonia, empyema, and other complications of bacteremia.

In a review of the literature on this subject, one is impressed with the comparative dearth of material and the infrequency with which articles have appeared in our journals.

I desire therefore to report the following case of puerperal sepsis, treated at the Beth-El Hospital, Brooklyn.

Case 89599.—L. Z., aged 22, white, primigravida, ante partum course essentially negative. Pelvic measurements relatively ample. Past medical history negative except for appendectomy about one year prior to present pregnancy, with uneventful convalescence. On Aug. 6, 1937, after a labor of nine hours and fifty minutes, patient was delivered spontaneously of a living male baby (weight 6 pounds, 14 ounces) in L.O.A. position. A right mediolateral episiotomy was repaired. At the end of labor, temperature 100.4° F., pulse 68, respirations 22, blood pressure 100/80. After thirty-six hours, patient had a chill, complained of soreness throughout the body, associated with a dry hacking, unproductive cough. Temperature 103.4° F., pulse 120, respirations 24. Physical examination at this time revealed no intra-abdominal or intrathoracic lesion.

Second day after delivery: Temperature 107.2° F., pulse 100, respirations 28. Medical examination was negative except for moderate tenderness in both lower quadrants. Urinalysis negative. Lochia foul. R.B.C. 3,500,000, Hg. 70 per cent, W.B.C. 18,000. Polymorphonuclears 84 per cent and monocytes 16 per cent. Blood culture (aerobic) negative after forty-eight hours.

Third, fourth, fifth days after delivery were marked by severe chills, occurring as often as every eight hours, followed by temperatures ranging from 105° to 108.4° F. In spite of this hyperpyrexia, the patient did not appear to be acutely ill, except for labial cyanosis. A second aerobic blood culture proved negative. Repeated physical examinations were negative.

On the sixth day, anaerobic blood culture was returned *positive* for *anaerobic hemolytic streptococcus*. General condition remained the same for the seventh day, averaging two to three chills within twenty-four hours. However, on the eighth day, the patient was seized with a sharp stabbing pain, in the left axilla, radiating to the left shoulder. Patient became cyanotic and dyspneic and was racked by a paroxysmal cough, followed by a sanguineous expectoration. Examination revealed fine and coarse râles in the left axilla and a pleural friction to-and-fro rub. Impression: pulmonary embolism. The pulmonary distress and cyanosis made it imperative that the patient be placed in an oxygen tent for relief. For the next nine days the chills were neither so severe nor the temperature so high. On the eighteenth day, the following physical signs indicated a left pyopneumothorax. The patient was dyspneic, moderately cyanotic and extremely pale. The left chest was completely tympanitic with absence of vocal fremitus and breath sounds, anteriorly. Posteriorly and in the lower left axilla there was cavernous breathing and a metallic tinkle as well as a succussion sound. The area of cardiac dullness was tympanitic and the heart was displaced to the right. A needle was inserted in the left eighth interspace, at the angle of the scapula and 1,100 c.c. of a grayish purulent fluid with distinct putrid or colon odor was removed. Portable roentgenograph showed "a collapse of a hydropneumothorax on the left side with a fluid level extending from the base upward to the second interspace. The heart and mediastinum are displaced to the right. There is a proliferative infiltration noted throughout the right pulmonic field, mainly in the region of the right middle lobe, suggestive of bronchopneumonia." Two days later, on the twentieth day of illness, an open thoracotomy was performed along the left seventh rib. A large empyema cavity was found extending from the second interspace to the diaphragm, filled with putrid yellow pus. Culture of the pus revealed a mixed aerobic and anaerobic infection, but no hemolytic streptococcus.

The same general condition prevailed for the next thirteen days, chills, hyperpyrexia (in spite of the ample drainage from the thoracotomy), moderate dyspnea and occasional cyanosis. At this time, blood culture became negative and patient showed signs of improvement, which continued until the patient's discharge on the sixty-second day of illness and forty-two days after the thoracotomy.

Prontosil and prontosil were used, but we were compelled to discontinue their use because of occasional attacks of cyanosis which may have been caused by the pulmonary complications and not by sulphhemoglobinemia. Blood transfusions were employed but with little apparent effect. Total of 1,350 c.c. of whole blood in doses of 150 c.c. were given by the citrate method, particularly at the onset. Rivanol, one of the aniline dyes, much in vogue in the 1920's, was also utilized in an effort to combat this condition, but to no avail. All known methods of treatment had apparently been useless. Therefore, with a hope that so-called specific therapy might be effective, we obtained and injected intramuscularly convalescent scarlet fever serum, in doses of 50 c.c. every eight hours, for a total of 1,560 c.c.

I wish to express my deep appreciation of the hearty and willing cooperation of Dr. S. Levine of the Medical Department and Dr. B. Kogut of the Surgical Service in the treatment of this case. Also my thanks to Dr. A. Koplowitz for his permission to report this rare and interesting case from his service.

REFERENCES

- Bondy*: Monatsschr. f. Geburtsh. u. Gynäk. 34: 536, 1911. *Schottmüller*: Mitt. a. d. Grenzgeb. d. u. Chir., Jena 21: 450, 1910. *Schwarz and Dieckman*: AM. J. OBST. & GYNEC. 13: 467, 1927. *Schwarz and Brown*: Ibid. 31: 379, 1936. *Schwarz and Dieckman*: South. M. J. 19: 6, 1926. *Colebrooke and Hare*: J. Obst & Gynaec. Brit. Emp. 40: 609, 1933. *Colebrooke, L.*: Lancet 1: 1085, 1935. *Burt-White, H.*: Lancet 1: 16, 1930. *Lash, A. F.*: AM. J. OBST. & GYNEC. 17: 297, 1929. *Idem*: J. A. M. A. 105: 29, 1935. *McDonald et al.*: Arch. Path. 23: 230, 1937. *LeLorier, Dalsace, and Mayer*: Bull. Soc. d'obst. et de gynéc. 21: 93, 1932. *Oginz*: Am. J. Surg. 7: 647, 1929.

201 EASTERN PARKWAY

APLASIA OF THE LOWER FEMALE GENITAL TRACT

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AN UNDERSTANDING of developmental anomalies and malformations of the lower genital tract of the female must of necessity take in account embryology. Four conceptions, namely, (1) that the lower vagina and hymen are Müllerian in origin; (2) that they are Müllerian and Wolffian in origin; (3) that they are totally derived from the urogenital sinus; (4) that they are Müllerian and urogenital, have been considered. Koff¹ has recently reviewed the literature and has presented excellent evidence from studying human fetuses that the upper four-fifths of the vagina are Müllerian in origin and that the lower fifth and the hymen are formed from the Müllerian ducts and the sinovaginal bulbs, the latter arising from the epithelium of the urogenital sinus. The hymen is made up of two lateral lips and an inferior segment. The inferior segment is disc-like. Internally it is lined by stratified squamous epithelium of the vagina and externally by the stratified columnar epithelium of the urogenital sinus. Between these two epithelial coats is the compressed stroma of the vagina and urogenital sinus. Koff's¹ conception of the embryology of this part of the female genitalia seems clear-cut, and the following case is presented as a developmental anomaly based on his findings.

The patient is a forty-year-old single female who complained of irregular and profuse menstruation for the past three months. Bleeding was accompanied by the passage of clots, bright red blood, and dysmenorrhea, none of which she had previously experienced. There were no menopausal symptoms or symptoms of hypothyroidism. Neither was there any other vaginal discharge. Local examination revealed normal appearing external genitalia. Further inspection showed no hymenal opening and a urethral meatus somewhat larger than normal. A catheter was in-

serted in the bladder and a probe guided in the same orifice posterior to the catheter and in the direction of the cervix. By rectal examination it was followed from the region of the cervix to near the obstruction, which felt about one-half inch thick. By rectal examination the cervix felt longer than normal, the uterus and appendages being normal. The patient was instructed to return for further examination at the next menstrual period. Inspection at this time showed menstrual blood coming from the apparent urethral meatus. The patient entered the hospital following the period of bleeding. Examination under anesthesia was essentially as noted above. A small dilator was placed in the sinus leading toward the cervix. With this as a guide, a small anteroposterior incision was made in the occluding tissue. By means of blunt and sharp dissection the incision was deepened until the posterior wall was penetrated. The little finger was inserted and revealed normal vaginal tissue. The dilator was brought into view and dissection carried out anteriorly until the dilator was freed. Inspection showed the urethral meatus to be recessed some-

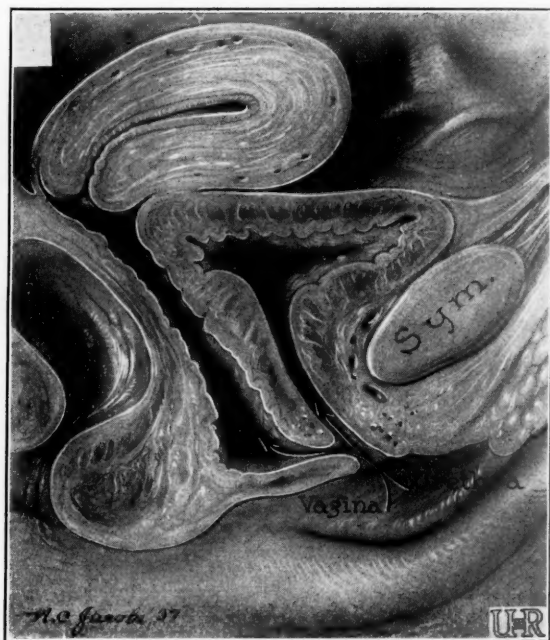


Fig. 1.

what on the anterior vaginal wall. The excess tissue which was about three-eighths of an inch in thickness was trimmed and the raw edges approximated with sutures. A dilatation and curettage was done in the usual manner. The cervix was longer than normal, otherwise the internal genitalia were not remarkable. Subsequent follow-up showed a good reconstruction. (See Fig. 1.)

DISCUSSION

The possibilities for explaining this anomaly from the embryologic point of view are first, that the posterior bulbous portion of the hymen grew too far toward the urethra and that the lateral slits formed by the invagination failed to materialize, the inferior aspect of the hymen proliferating abnormally. Second, the fusion of the proliferating vaginal epithelium and urogenital sinus failed, and third, the plug of vaginal epithelium, which normally proliferates eccentrically and posteriorly, proliferated only toward the urethra. That the case presented is not an imperforate

hymen is shown by the fact that menstrual blood escaped through the apparent urethral meatus, and had the hymen been imperforate, the patient would have had a hematoocolpos in her early menstrual life. McKelvey and Baxter² presented a case of marked developmental anomaly, part of which showed the vagina ending in a blind pouch caudally. This part they claim had all the characteristics of normal vaginal tissue. They fit their finding to Koff's¹ conception or that of Mijsberg³ the latter claiming that the lower part of the vagina is Wolfian in origin. Masson⁴ illustrates a case similar to the one presented. In his case there is less vagina caudally and a sinus connecting the vagina cephalad to the urethra. Similar anomalies occur in female pseudohermaphrodites and hermaphrodites of undetermined sex.⁵

CONCLUSIONS

A case of aplasia of the lower female tract is presented which is believed to be due to a failure of the proliferating epithelial plug of the vagina to grow posteriorly and a failure of fusion with the sinovaginal bulbs. That the inferior aspect of the hymen enters into the formation of the anomaly cannot be doubted.

REFERENCES

- (1) Koff, A. K.: Contributions to Embryology 24: 61, 1933. (2) McKelvey, J. L., and Baxter, J. S.: AM. J. OBST. & GYNEC. 29: 267, 1935. (3) Mijsberg, W. A.: Quoting McKelvey and Baxter, Ztschr. f. Anat. 74: 684, 1924. (4) Masson, J. C.: Obstetrics and Gynecology, Curtiss 3: 670, 1933. (5) Young, H. H.: Genital Abnormalities. Hermaphroditism and Related Adrenal Disease, Philadelphia, 1937, The Williams & Wilkins Co.

SEGMENTAL TORSION OF FALLOPIAN TUBE IN A YOUNG VIRGIN*

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TORSION in the Fallopian tube is uncommon and especially rare in the virgin. A review of the literature by McEachern in 1934, revealed only 9 cases. Additional cases in virgins are recorded by Stark, Davies, Rogers, Darnier, Jefferson, Gillies, Corlette, Michon, Block, and Michael. A study in December, 1935 made by K. F. D. Waters revealed 17 recorded cases of tubal torsion in young girls, although in this paper virginity was not a prerequisite.

In the case abstracted below torsion has evidently occurred in a normal tube. This inference is supported by the age of the patient, virginity, and findings at operation.

Miss M. E., aged 19 years, single, was admitted to the Greenpoint Hospital on Feb. 17, 1937, complaining of pain in the left lower quadrant. Childhood diseases included diphtheria and scarlet fever. Menstruation began at the age of thirteen, was always regular and of a twenty-eight day type, and of three days' duration. The patient had typhoid fever in March, 1936 and was in bed for four weeks. This was followed by a period of amenorrhea for two months. Menstruation resumed in May, 1936 was accompanied by severe cramplike pains localized to the left lower quadrant. Since then, menstruation has occurred every twenty-one days, for six days. Pain in the left lower abdomen has since appeared three days prior to menstruation, persisting until two days after completion of bleeding.

Upon admission the temperature, pulse, and respirations were normal. Head, neck, and thorax revealed nothing of note. The abdomen presented an insensitive mass,

*Presented at a meeting of the Brooklyn Gynecological Society, March 4, 1938.

2 or 3 cm. above the left Poupart's ligament. This was dull to percussion but sensitive to touch. Pelvic examination revealed an intact virginal introitus. On rectal palpation the cervix was found to point anteriorly. The uterus was normal in size, retroverted and crowded over to the right. A tense, cystic globular mass about 6 or 7 cm. in diameter filled the left fornix and encroached upon the cul-de-sac. The laboratory data were not unusual. A diagnosis of left ovarian cyst was made.

Under ether anesthesia laparotomy was performed on Feb. 24, 1937 through a mid-line scar 10 cm. in length. About 30 c.c. of serosanguineous fluid was found free in the pelvic cavity. The uterus was small and pubescent. The right tube and ovary were normal. A Morgagni cyst about 2 cm. in diameter was found in the outer end of the right broad ligament. The left tube was converted into a retort-shaped structure, the dilated ampullar segment measuring about 5 cm. in diameter. Two twists were found at the junction of the middle and outer thirds of the tube, just external to the outer edge of the mesovarium. The wall of the tube distal to the site of strangulation was dark and hemorrhagic, the remainder was normal in color and appearance. The left ovary was normal in size and color. The left tube was untwisted, resected, and excised at its interstitial portion. The normal left ovary was retained. The raw surfaces were peritonized by the round ligament and the left ovary suspended. The Morgagni cyst on the right was resected and the posterior leaf of the broad ligament closed. The postoperative course was uneventful.

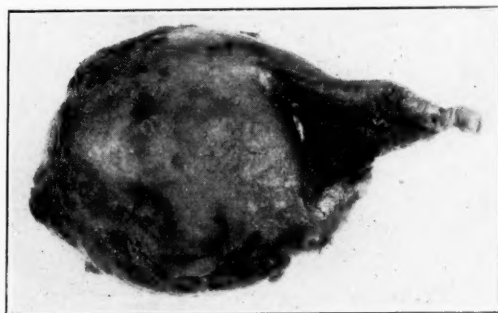


Fig. 1.—The tube is enlarged and dilated in its outer third. In this zone the color is blue black, the peritoneum lusterless.

The pathologic report follows: The specimen consisted of a retort-shaped tube measuring 13 cm. in length, 5 mm. at the uterine insertion and 6 cm. in diameter in its distal third (Fig. 1). The external appearance was varied. The inner two-thirds of the tube presented a smooth shiny peritoneal coat which was somewhat injected. At the junction of the middle and outer thirds there was marked angulation. The twist previously described at this point was not well defined, probably the result of operative handling and fixation. The outer third of the organ was hemorrhagic, blue gray, and lusterless. The fimbriae were retracted and the abdominal ostium as such was no longer recognizable.

The mesosalpinx in this zone was thickened and hemorrhagic. On section the dilated tubal segment was filled with blood which shelled easily from the underlying endosalpinx. The latter was smooth and blue gray in appearance. All folds had been obliterated. The tubal musculature was hemorrhagic and markedly atrophic. Through the inner two-thirds the lumen was normal and free from blood. The folds were grossly normal. The muscle was slightly edematous. The serosa was injected. Microscopically, section through the isthmus segment of the tube also included a zone of the muscular coat of the uterus. The tube lumen though narrow was normal and free from blood. The folds were short. The inner longitudinal muscle coat was well defined. The broad circular muscular coat was sharply differentiated and in turn was succeeded by a second longitudinal coat which fused with the uterine musculature. A zone of loose areolar tissue, however, intervened. This contained several vessels

about which were collections of lymphocytes especially prominent about the veins. The muscle fasciculi of the uterus showed slight edema and capillary engorgement. Just beneath the perimetrium the capillaries contained an occasional polymorphonuclear leucocyte. About them too were moderate numbers of lymphocytes and occasional plasma cells. In the outer segment of the tube, distal to the point of torsion, the tube lumen was widely dilated. All the folds had been obliterated (Fig. 2). The lining epithelium and muscle fasciculi were all necrotic for the nuclear elements had disappeared and only cell shadows remained. Edema was evidenced by wide separation of the muscle cells and the presence of granular fibrin between the interstices. At the periphery a narrow segment of viable muscle and connective tissue fibers was found. Zones of interstitial hemorrhage were present. An occasional lymphocyte was encountered. The detached blood clot found in the tube lumen was free from chorionic villi. Torsion and necrosis of the distal third of the tube found at operation was accordingly confirmed. Inflammatory reaction in the viable segment was evidently secondary.

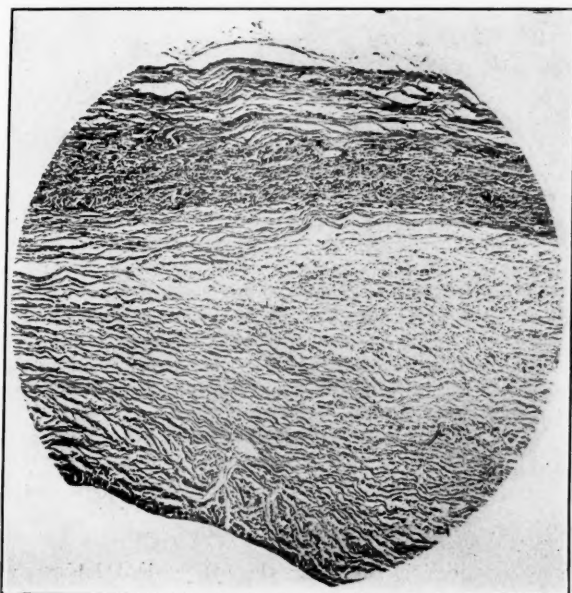


Fig. 2.— $\times 80$. A segment of tube wall through the dilated and necrotic ampullar zone. All folds have been obliterated. The muscle and connective tissue fibers are necrotic, only the cell shadows remain. No exudate is present. The blood clot was artificially removed from the tube lumen.

In retrospect, this case may be considered as one of torsion beginning with the first menstruation after an attack of typhoid fever, terminating in complete necrosis of the twisted segment. Pre-existing inflammation was not a factor, for the hymen was found intact and no pathology was present in the uterus and right adnexa. Furthermore the involved tube showed no evidence of inflammation in mucosa or muscle proximal to the site of occlusion.

CONCLUSIONS

A case of segmental torsion and necrosis of the left tube occurring in a virgin is herein recorded. The onset was sudden in the early menstrual phase. The left sided pain recurred monthly until admission to the hospital. A twisted tube with two complete turns at the junction of the middle and outer thirds was erroneously interpreted as an ovarian cyst. Pathologically, the dilated portion of the tube was the seat of an old hematoma and the wall was completely necrotic distal

to the site of torsion. There was no evidence of inflammation. The opposite adnexa were normal. This case may be therefore viewed as one of segmental torsion and necrosis of a previously normal tube occurring in a young virgin.

1530 PRESIDENT STREET

MELANOMA OF THE VULVA*

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(From the Department of Gynecology of the Elizabeth Steel Magee Hospital and the University of Pittsburgh.)

DURING the past year it has been the writer's good fortune to chance upon a very infrequent type of malignancy of the vulva, namely, malignant melanoma.

Mrs. M. I., a 76-year-old white woman, was seen in the Magee Dispensary complaining of "lumps" in the vulva and both inguinal regions. The patient stated that she had always had a small mole on the right labium majus. In October, 1932 she first noticed black "lumps" on the right vulva, which were painless. Four months later they began to bleed and were considerably larger. On Feb. 13, 1936, "lumps" were observed in the right groin, following three operations a month previously under local anesthesia. Six weeks before admission the patient felt additional "lumps" in the left groin. At this time she had had a serosanguineous vaginal discharge for about eighteen months. The "lumps" had been painful for about two years and were becoming progressively larger. She had lost only a slight amount of weight. Associated symptoms included headache, blurring of vision, tinnitus, and episodes of abdominal discomfort following ingestion of fried foods. The menstrual history was normal and the menopause occurred at the age of fifty. She had had two normal full-term pregnancies. The past medical history included typhoid, measles, influenza, and diphtheria. The family history was negative for malignancy.

There was marked wrinkling of the skin. The vessels were hard, tortuous, and sclerosed. She had complete dentures. The tonsils were enlarged. The heart was not enlarged but a few premature beats were noted. There was slight pretibial edema.

The vulvar lesion (Fig. 1) consisted of a large somewhat nodular mass, irregularly the size of a tangerine, occupying the entire right labium minor and of a purplish color. The lower surface of the mass presented some ulceration and extended out to the clitoris, prepuce, upper part of left labium minor, and had infiltrated through so that there were several pigmented spots, of various sizes, on the outer surface of the right labium major. There were large firm masses in both inguinal regions.

Laboratory findings.—The urine was negative except for a few white blood corpuscles. It was negative for melanin. Blood count: R. B. C., 3,690,000; W. B. C., 5,550; polymorphonuclears, 56 per cent; lymphocytes, 43 per cent. The blood sugar was 120 mg. Nonprotein nitrogen was 24.3 mg. Kahn was negative. Sedimentation time was 20 min.

Course in hospital.—On Dec. 21, 1936, under gas-ether anesthesia a biopsy was taken and four radium needles, containing $12\frac{1}{2}$ mg. of radium each, were inserted directly into the vulvar mass, for a period of forty-eight hours (2,400 mg. hr. of radiation).

Pathologic Report From Biopsy.—The tumor (Fig. 2) was composed of a pleomorphic type of cell, varying from spindle cell type to a large epithelial type. The cells varied in their melanin content, some of them being melanin free, and others

*Read at a meeting of the Pittsburgh Obstetrical and Gynecological Society, February 7, 1938.

so packed with pigment that the cell outline was lost. There were areas of necrosis, but for the most part the tumor was quite cellular. With the Wilder silver stain, some of the spindle-shaped cells had fibrils, while other cells were devoid of fibrils. The fibril-free cells predominated. The distribution of the pigment varied in different cells, some of the cells being so packed with pigment as to render obscure the cell outlines, while other cells were devoid of pigment.

Diagnosis: Melanoma of the vulva.

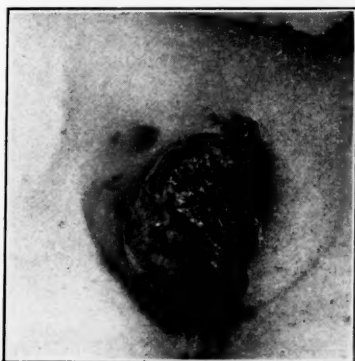


Fig. 1.

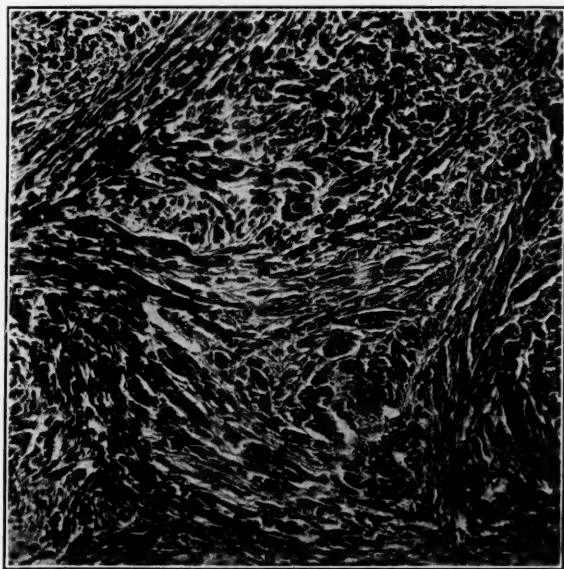


Fig. 2.

Following radiation, the mass seemed to shrink to about two-thirds of its former size and was the seat of a profuse seropurulent exudate, with the patient experiencing considerable discomfort in this area. On Jan. 17, 1937, under nitrous oxide anesthesia, radium needles were again inserted, this time around the periphery of the tumor and allowed to remain in situ for forty-eight hours (2400 mg. hr. of radiation). Symptoms continued practically the same, the patient losing ground very rapidly. On Feb. 10, 1937, about seven weeks after the initial radiation, due to the extreme discomfort of the lesion to the patient, it was decided to excise as

much of the growth as possible. Accordingly, under gas anesthesia, a cautery excision of the growth was performed. During the procedure, all areas where the melanoma had reached the surface, were fulgurated with the electric current. Following the operative procedure, the patient was more comfortable, but continued to lose considerable weight and developed a moderately severe cough. On Feb. 21, 1937, the patient began to develop symptoms of pulmonary congestion and thereafter the course was progressively downward and terminated in death on March 1, 1937.

Autopsy revealed melanoma of the vulva with metastases to inguinal lymph nodes, lungs, stomach, and pancreas. Both lungs were riddled with tumor nodules which varied in size from that of a pea to that of a plum. The metastasis to the stomach consisted of a small, flat, white nodule on the greater curvature. The metastasis to the pancreas was not seen in the gross examination of the organ, but microscopically consisted of a circumscribed mass of tumor tissue in which the cells were spindle shaped. In the lymph nodes, the lymphoid tissue was entirely replaced by tumor, with large areas of hemorrhage and necrosis.

Acknowledgement is here made to Dr. B. Z. Cashman for permission to report this case; to Dr. Mortimer Cohen for the pathological data; and to Miss Ann Shiras for the photographs.

3710 FIFTH AVENUE.

CARCINOMA OF THE CERVIX DURING PREGNANCY*

SAMUEL GOLDSTEIN, B.S., M.D., F.A.C.S., PITTSBURGH, PA.

CARCINOMA of the cervix, being found so rarely as a complication of pregnancy, especially in women who are pregnant for the first time, prompted us to report this case.

CASE J-6234.—A white patient, E. P., aged 22 years, was admitted to the Gynecological Service of Dr. T. B. Carroll in the Montefiore Hospital on Aug. 27, 1937. She was seen the week prior in the Obstetrical Out-patient Department. Her chief complaint was that one week before admittance to the hospital, she had noticed spotting after coitus for the first time. This bleeding was painless.

For a month or so prior to this, she had noticed a white vaginal nonodorous discharge. Her menstrual history showed nothing irregular. Puberty occurred at sixteen years of age, her periods being regular, every twenty-eight days, lasting five days, and of moderate amount. Her last menstrual period was on Feb. 19, 1937 and of the usual duration. Patient had been married one year and had never been pregnant before. No history of abortions or miscarriages. Her family history showed no evidence of cancer or tuberculosis. Her father and mother, two brothers, and two sisters, are all living and well.

Abdominal examination revealed the abdomen enlarged to the size of about six months' pregnancy. The baby was in R. O. A. position with fetal heart sounds heard in the right lower quadrant.

Vaginal Examination: Attached to the anterior lip of the cervix was a soft, friable, everting, cauliflower, vascular mass, the size of a lemon, attached by a short pedicle. The uterus was not fixed, the fornices were clear, and the tumor with the cervix could be delivered entirely outside of the vagina. At first, one thought of the possibility of malignant degeneration of a cervical polyp.

On Sept. 2, 1937 the patient was operated upon and the mass was removed with its small pedicle with the actual cautery. On Sept. 7, 1937 patient was in excellent condition but said that she felt no fetal movements. Fetal heart sounds could not be heard. On Sept. 9, 1937 patient delivered herself of a macerated fetus, spontaneously, with no complications. On Sept. 20, 1937 patient received a course of

*Read at a meeting of the Pittsburgh Obstetrical and Gynecological Society, February 7, 1938.

deep x-ray therapy. She was instructed to return in a month for radium treatment. The patient, however, was noncooperative and, in spite of urging by the social worker, did not return until Dec. 21, 1937. She was then given 3,600 mg.



Fig. 1.—Cauliflower-like tumor mass, measuring 6 by 5 by 4 cm. with a pedicle, removed with the cautery.



Fig. 2.—High Power 400X H. E. Showing large undifferentiated epithelial cells, hyperchromatic nuclei, few mitoses, vacuolated cytoplasm.

hr. of radium. Examination at that time revealed the cervix healed, uterus in anterior position, normal size, and freely movable, with the fornices clear. The blood count was within normal limits, urethral smear was negative for gonococci. The blood Wassermann was negative.

Pathological Report, by Dr. K. Yardumian: Gross Findings: The specimen consisted of a tumor mass, measuring 6 by 5 by 4 cm. with a pedicle. It was cauliflower-like, soft and friable in consistency, pinkish gray in color, showing areas of hemorrhage.

Microscopic Findings: Sections of the tumor showed various pictures in different parts of the tissue. There were areas highly vascular with poorly defined vascular walls with very little stroma. The cells were vacuolated, multiform, with a tendency to form giant cells, while in other parts there were islands of cells with tendency to form acini. Cells were uniform in size, hypochromatic nuclei, and numerous mitotic figures. There were strands of fibroconnective tissue, separating the acini. The general picture of the tumor was that of a very fast growing adenocarcinoma with areas resembling sarcomatous degeneration. However, this might have been due to the rapid course of the tumor.

Diagnosis: Adenocarcinoma of the cervix (embryonic in type).

NOTE: Since this report was submitted, the patient was seen in the clinic on March 11 and April 8, 1938. She had no complaints and was in excellent health, having gained four pounds. Pelvic examination revealed no evidence of metastasis, the cervix was clean and healed, the uterus in anterior position and freely movable, and of normal size and consistency. The parametria were free.

I wish to thank Dr. T. B. Carroll for permission to report this case and for his helpful suggestions in the treatment.

4135 JENKINS ARCADE

TORSION OF THE FALLOPIAN TUBE*

SANFORD KAMINESTER, M.D., F.A.C.S., BROOKLYN, N. Y.

THE present case, in which torsion was produced by a small parovarian cyst, is reported simply to bring to mind the possibility of this condition existing in all cases of obscure intra-abdominal disturbance in the female.

Mrs. L. S., married, white, was seen in consultation on Jan. 11, 1937. She was 24 years of age and had been married for four years. At about the time of her marriage she had been operated upon for appendicitis. She had been pregnant once and had been delivered of an average size child two years after her marriage. One year before the occurrence of the present illness the patient had had an attack of pain in the left lower quadrant which had subsided after twenty-four hours without treatment.

On Jan. 9, 1937, there had been an attack of severe pain over the left lower quadrant associated with vomiting. This pain continued with remissions for two days, at which time hospitalization was advised. The menses had always been regular and the last period had occurred on Dec. 25, 1936.

Examination revealed a well-nourished, well-developed adult female who was suffering intensely. Temperature was 101.4° F., pulse 90, respiration 22, and blood pressure 124/80. Abdominal examination showed a well-healed, right rectus scar and also revealed marked tenderness in the left lower quadrant associated with rebound tenderness. On pelvic examination there was no bleeding. The cervix was in position and very painful on attempted motion. The uterus could not be definitely made out due to the abdominal spasm and tenderness. In the left fornix there was a very tender, irregularly shaped mass.

The urine was normal. Blood examination showed 9,750 white blood cells, with 72 per cent polymorphonuclear leucocytes.

A preoperative diagnosis of torsion of an ovarian cyst or hemorrhage from a ruptured follicle was made and laparotomy decided upon.

*Presented at a meeting of the Brooklyn Gynecological Society, March 4, 1938.

Under spinal anesthesia, the abdominal cavity was opened. The left tube was found in the cul-de-sac. It was freely movable and could easily be delivered into the wound. The distal half of the tube was swollen and hemorrhagic and almost black in color. It had twisted 180 degrees, this twist being produced by a small cystic tumor which was attached to the mesosalpinx by a fibrous band. The ovary was not involved. The right tube and ovary appeared normal. The left tube and ovary were removed, care being taken to transect through normal tissue to avoid the possibility of cutting through thrombosed vessels. Convalescence was uneventful.

Examination of the removed specimen showed the tube to be 9 cm. in length, 2 cm. in diameter at its fimbriated end and 4 mm. at the proximal end. The outer

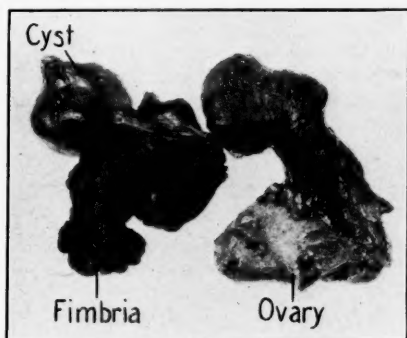


Fig. 1.—Showing torsion of tube due to ovarian cyst.

half was deeply hemorrhagic and swollen, although the fimbria were still distinct and the abdominal ostium patent. Attached to the mesosalpinx was a cystic structure measuring 2 by 3 cm. in diameter. This structure had caused beginning necrosis of the tube by strangulating it at its mid-portion. The wall of the cyst measured 3 mm. in thickness and was infiltrated with blood. The ovary, which measured 3 cm. in diameter, was normal on gross and microscopic study. The proximal part of the tube showed edema and some infiltration of the wall with polymorphonuclear leucocytes. The distal portion and the wall of the cyst were so hemorrhagic that no further detail could be made out.

340 ST. JOHNS PLACE

ATRESIA OF THE VAGINA*

JOSEPH L. BAER, M.D., CHICAGO, ILL.

THE following case report deals with a complete atresia of the upper two-thirds of the vagina, i.e., that portion of the vaginal tube which arises from the fusion of the lowermost parts of the Müllerian bodies.

The patient, E. M., aged 16 years, had never menstruated. Her identical twin sister had menstruated more or less normally for approximately two years. The girl was seen by the school physician who found a mass in the abdomen. She was then brought to me. On examination the external genitalia were normal. It was possible to insert the first phalanx past the intact hymen into a closed pouch, the depth of which was no greater than 2 cm. On rectoabdominal examination the mass which the school physician had felt was about the size of a four months'

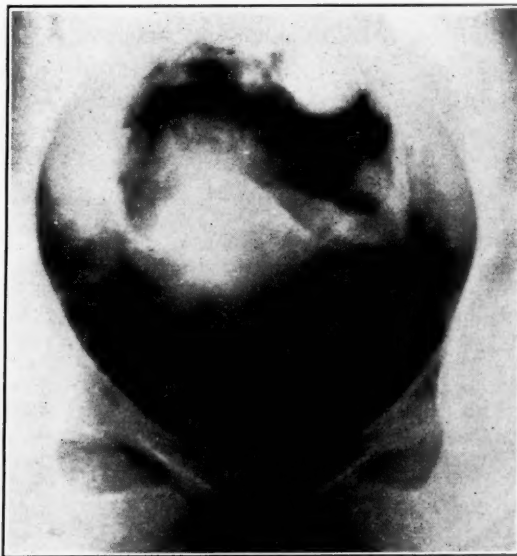


Fig. 1.—Pelvic roentgenogram by transabdominal pneumoperitoneum showing uterine mass with a more opaque core (hematometra).

pregnancy, with something of the outline of the uterus, freely movable, insensitive and with a tapering lower pole. An intravenous pyelogram was made to make sure there was no anomaly of the urinary system, and then a transabdominal pelvic roentgenogram was made, in order to determine the amount of tissue that lay between the lower pole of the mass and the apex of the exceedingly small vaginal tube. The approximate distance between this tiny vaginal vault and the lowermost pole of the uterine mass was 6 cm. Evidently only the ectodermal invagination had taken place. The denser shadow within the uterine mass was interpreted as retained menstrual blood.

There are two surgical approaches to this problem, one, vaginal, the other abdominal. In the literature two points are emphasized; first, that if possible, where there is functioning endometrium it is desirable to establish menstruation by connecting the blind lower uterine pole with the vaginal pouch; second, in the adolescent

*Presented at a meeting of the Chicago Gynecological Society, December 17, 1937.

girl it is highly desirable to do nothing more, but to await marriage. If the tiny vaginal tube remains inadequate for coitus and it becomes necessary to do a vaginal plastic operation, then marital coitus is essential to the permanent success of the plastic operation. So in this instance the vaginal approach was selected.

Under ethylene-oxygen anesthesia the apex of this tiny vaginal vault was split transversely, and then with a sound in the urethra and bladder and the assistant's finger in the rectum, we proceeded with blunt and sharp dissection through the rectovaginal tissue. Meanwhile abdominal pressure was made to bring the lower pole of the mass somewhat closer to the cul-de-sac. Eventually it was possible to grasp the lower pole with a tenaculum, and then with a little further blunt dissection a single droplet of black, thick fluid appeared, obviously some retained menstrual blood. With sound exploration the canal of the cervix was identified and dilated.

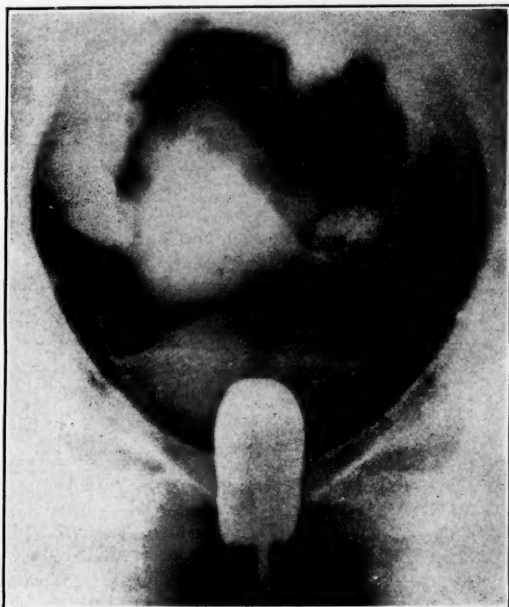


Fig. 2.—Same plus visualization of hypoplastic vaginal pouch distended by opaque medium. Note the distance between the vaginal vault and the uterine mass.

Approximately 10 to 12 ounces of retained black menstrual blood escaped. The so-called cervix was then brought down to the level of the little vaginal vault where it was anchored with mattress sutures. The girl made an uneventful convalescence. The date of the operation was October 16 and last week, December 10, she had her first normal menstrual period.

The abdominal approach in these patients is distinctly unsatisfactory. The depth of the cul-de-sac and the dissection necessary to reach such a tiny vaginal pouch from above is obviously more difficult than the approach from below. However, if the all-important preliminary intravenous pyelogram reveals possible involvement of one or both ureters in the anomalous development, then the abdominal approach becomes the safer route.

A CASE OF SECONDARY ABDOMINAL PREGNANCY*

CRAIG WRIGHT MUCKLE, M.D., PHILADELPHIA, PA.

(From the Philadelphia Lying-In Hospital)

THE value of the diagnostic methods utilized in the following case of abdominal pregnancy seems to warrant its presentation.

M. M., a 25-year-old negress, was admitted to the Pennsylvania Hospital on May 22, 1937. Menstruation began at the age of thirteen years, occurred regularly every twenty-eight days, lasting three and a half days and was accompanied by cramps at the onset. She was married in June, 1933; was delivered of one child by breech extraction in October, 1936. The last menstrual period prior to admission began on Dec. 2, 1936 and lasted three days.

From the middle of December, until her admission, she had been more or less constantly troubled by distention, gaseous eructation, and constipation.

On Jan. 17, 1937 she was admitted to another hospital for six days because of vomiting, obstipation, and swelling of the abdomen. She improved rapidly under conservative treatment and was discharged with the diagnosis of autointoxication.

On May 9, 1937 vaginal bleeding began and the following day the patient passed a piece of tissue three inches long which she said "looked like a dog's tail." Slight vaginal bleeding continued for a period of ten days. She was admitted to the hospital on May 22 because of abdominal distention, vomiting, and constipation. The temperature was 99.2° F.; pulse and respirations, normal. The abdomen was tense, swollen, and signs of free peritoneal fluid were present. The abdominal enlargement was symmetrical and a mass was felt extending from the symphysis to a point one fingerbreadth below the umbilicus. There was moderate tenderness but no rigidity. On examination the vaginal mucosa and cervix were soft and cyanotic. No adnexal masses were felt. There was no vaginal bleeding. The blood count was 2,900,000 red cells; 6,800 white cells, hemoglobin 8 gm.; the differential count was normal.

On admission the tentative diagnoses were intrauterine pregnancy of five months' duration or hydatidiform mole.

The Friedman test was positive but a quantitative determination revealed no excess of prolactin.

The piece of tissue which had been passed spontaneously was examined by Dr. Robert F. Norris, who submitted the following report:

"The tissue in formalin was cylindrical and measured 6 cm. by 2 cm. It was reddish brown in color with a rough granular surface. Grossly it appeared to be a cast of necrotic tissue from the uterine cavity. Microscopically the tissue was somewhat autolyzed and consisted entirely of decidual cells with pink cytoplasm and large dark staining nuclei which appeared normal. There was no variation in the size, shape, or staining qualities of the cells. No chorionic villi were seen. The presence of decidual tissue without chorionic villi suggests the possibility of an extrauterine pregnancy. *Diagnosis:* Decidual cast from uterine cavity."

The history of amenorrhea and the size of the abdominal tumor indicated pregnancy. This was confirmed by a positive Friedman test. Abdominal distention and pain constituted the chief complaints. The absence of chorionic villi in the decidual cast suggested extrauterine pregnancy.

On x-ray examination, Dr. Paul Bishop submitted the following report:

"There is a single fetus lying transversely across the upper abdomen, the head to the maternal left side, the buttocks to the right. The stomach is displaced upward, the transverse colon downward and the fetus does not seem to be connected with the uterus." In conference, Bishop pointed out that a loop of intestine was lying *below* the fetus instead of being displaced upward by the growing uterus.

To clarify the diagnosis, an x-ray study was made after intrauterine injection of iodized oil:

"On the injection of lipiodol the uterus is found to be slightly larger than the average nongravid uterus and tilted toward the left side. The fetus is found to

*Read at a meeting of the Obstetrical Society of Philadelphia, January 6, 1938.

be definitely outside the uterine cavity. No lipiodol has extended outward into the tubes."

Laparotomy was performed on May 27, 1937. The amniotic sac was adherent to the transverse colon. A stillborn, unmacerated fetus was removed. The placenta lay in a rent in the right Fallopian tube. The left tube and both ovaries were normal. The uterus was slightly enlarged. A supravaginal hysterectomy and right salpingectomy were performed. Maternal convalescence was uneventful.

SUMMARY

1. The patient was admitted because of abdominal pain and history of five months amenorrhea followed by vaginal bleeding.
2. The Friedman test was positive.
3. There were decidual cells present without chorionic villi.
4. Roentgenogram showed the fetus high in the abdomen.
5. Uterosalphingogram revealed the uterus only slightly enlarged and displaced downward and to the left.

CONCLUSION

Examination of tissue from the uterine cavity for the presence of chorionic villi, and uterosalpingography are two valuable aids in the diagnosis of abdominal pregnancy.

A PESSARY FOR MODERATELY-SIZED CYSTOCELES

CHENEY M. STIMSON, M.D., PHILADELPHIA, PA.

(From the Department of Gynecology, Jefferson Medical College)

THE illustration represents a modified Smith pessary, designed for the support of moderately-sized cystoceles. The modification differs from the regular Smith retro-displacement pessary, in that the smaller end, that which rests against the anterior vaginal wall, affords a solid surface, against which the cystocele may press. The vacancy, formerly enclosed at the smaller end of the pessary, is filled in with hard



rubber, the same as that used in the rest of the pessary. There should be left at the larger end, the lumen, sufficient room for the cervix, and for the bar to slip in place in the posterior fornix.

I have used sizes 0, 1, and 2, for moderately-sized cystoceles, where there was fairly good perineal support. In such cases this pessary proved quite satisfactory. But for the reason that perineal support is usually lacking in larger cystoceles, I have not tried larger sizes.

Special Article

THE INTRAVENOUS ADMINISTRATION OF POSTPITUITARY EXTRACT FOR OBSTETRIC PURPOSES

A NOTE ON THE TWENTY-FIFTH ANNIVERSARY OF THE INTRODUCTION OF THIS PROCEDURE

J. HOFBAUER, M.D., CINCINNATI, OHIO

"Finality is rarely attained in any field of human interest."

—LaFayette B. Mendel.

THERE is perfect unanimity regarding the unique merit of post-pituitary extract both for the initiation and stimulation of regular intermittent uterine contractions at term and during labor. While in the past the drug has been almost exclusively employed by subcutaneous injection, increased interest is being evidenced in recent years in its intravenous administration. It is my purpose in this communication to give a comprehensive review of the indications and contraindications of the use of this method for various obstetric conditions, as established by actual experience and also to correct certain recent misrepresentations.

In 1912, now twenty-six-years ago, the present writer advocated the intravenous administration of pituitary extract "when during labor an immediate and prompt response is essential."¹ In a more extended paper, the indications for this new method were discussed and a dose of two or three minims of the commercial preparation, routinely *diluted* with 1 c.c. of normal saline solution and to be injected slowly, was recommended.²

Abortion.—While in one of his early publications on the subject, the author emphasized that, for the induction of abortion pituitary extract is of no avail, its intravenous administration preceding intrauterine manipulations for emptying the uterine cavity, was found highly satisfactory. The fact that the wall of the pregnant uterus contracts rigidly in response to its intravenous injection, renders any attempt to remove the remnants of the product of conception instrumentally, easier and less risky, especially in less trained hands. In preference to the intravenous administration by an assistant, I, as a routine for the past few years, inject an ampoule of obstetric pituitrin *into the substance of the posterior lip of the uterine cervix* with uniformly satisfactory results. Vigorous spastic contractions of the uterine muscle ensues almost immediately. In our series of observations it was worthy of note that the wall of the uterine cervix remained unaffected, while the musculature of the fundus immediately responded to the intracervical injection of pituitrin. These clinical observations of the insensitivity of the uterine cervix to pituitary extract have, of late, been fully confirmed by Newton in experiments on laboratory animals.³

Induction of Labor.—While the oxytocic principle of the posterior pituitary lobe when given in *small doses* subcutaneously, renders valuable service for the induction of labor at term,² the intravenous administration of the drug for such purposes is to be deprecated on account of the not infrequent occurrence of tetanic contractions of the uterus, which

may persist for several minutes and seriously endanger the fetus. The nasal route, on the other hand, represents an appropriate procedure for the induction of labor in both normal and complicated cases.

Pyelitis.—Diminution of tone of the musculature of the ureter and ureteral dilatation were described by the author, in 1928, as constant concomitants of normal gestation. Impairment of the expulsive forces of the ureter in the gravid state, with the atony even more marked in the presence of superimposed urinary infection, was stressed as a definite impediment to the free discharge of urine, thus enhancing the risk of infection of the urinary tract and reducing its capacity to eliminate an actual bacterial infection.⁴

New efforts of therapeusis were based upon the observation in man and in animal experiments that the musculature of both the renal pelvis and ureter respond with peristaltic movements to pituitary extract.⁴ This drug was found to act even more definitely in the presence of considerable atony of the structures. The inference was obvious. Augmenting the tone and peristalsis of the ureter and, thus, accelerating the drainage of the atonic ureter in cases of pyelitis, appeared a rational procedure. The exhibition of solution of pituitary, and recently of pitressin, has proved useful in this respect. Our observations have been substantiated by Reiman,⁵ Jona and Flecker,⁶ DeLee,⁷ Stoeckel,⁸ Draper,⁹ Lower and Naujoks. Striking relief of pain, associated with objective improvement, and diminution of the abnormal elements in the urine, were apparent in the overwhelming majority of cases of pyelitis thus treated. Recently, we have combined with this treatment the oral administration of prontosil. In obstinate cases, when the subcutaneous injection of pitressin fails to remedy the situation, the intravenous route of administration has proved superior. Success was noted with this treatment in every case of pyelitis observed during the puerperium. Our experience demonstrates that in most instances of pyelitis in pregnancy ureteral catheterization can advantageously be obviated by the exhibition of a solution of post-pituitary, if combined with prontosil. For those rare cases which are not benefited by this method and require instrumental drainage, pituitary therapy as an additional measure, has proved of distinct advantage. Even after normal pregnancy, when during its course an undue number of leucocytes has been repeatedly observed, the exhibition of pituitary by the hypodermic or intravenous route, with a view to restoring the dynamics of the ureter to normal, is well grounded in actual practice.

Labor.—With the indications for the use of postpituitary extract during labor, I do not propose to deal in detail. The statement made in our first communications on the subject, that uterine inertia represents its principal indication, has withstood the test of time and progress.

Repeatedly we have warned that pituitary extract is out of place in the presence of cervical obstruction, overstretched lower uterine segment, manifest disproportion, rigid perineum; and also, that misapprehension of the obstetric situation and indiscreet dosage invite calamity. In other words, the use of this potent remedy should be tempered with judgment, proper regard for indication and dosage being most essential.

In my hands, the intravenous administration of one minim of solution of pituitary has proved serviceable during labor in cases which did not respond to the subcutaneous hypodermic administration of the drug.

Eclampsia.—The heightened response of the pre-eclamptic and eclamptic woman to posterior pituitary extract constitutes a contraindication to its employment. As observed in the previous paper on the subject,

generalized convulsions may occur in this group of patients following the exhibition of postpituitary preparations.¹⁰ Schoekaert recently observed severe convulsions in three pre-eclamptic women, following the administration of a few minims of postpituitary extract.¹³ In this conjunction, attention is called to my recent analysis of the hormonal aspect of the pathogenesis of eclampsia.¹¹

Cesarean Section.—Immediately after the delivery of the baby by cesarean section, I have routinely injected solution of pituitary into the cubital vein. The uterus blanches and remains firmly contracted. This procedure distinctly facilitates the insertion of sutures into the uterine wall. We feel that this method is in several respects superior to the intramural injection of postpituitary. Ergot is administered hypodermically as an efficient adjunct and safeguard, ten minutes after the intravenous administration of pituitary extract.

Anesthesia and Analgesia.—Anesthetics and analgesics (chloroform, ether, pantopon, morphine, chloral) in no way impair the effect of solution of postpituitary during labor.² In 1928, the rectal administration of amytal was introduced. Our observations of rapid cervical dilatation, considerable alleviation of pain, amnesia, regularity of uterine contractions have been confirmed by several investigators. The evidence now at hand shows that the postpituitary oxytocic effect is not abolished in the parturient woman by amytal or nembutal twilight sleep.

Placenta Previa.—Ante-partum bleeding in cases of low implantation of the placenta and of placenta marginalis may be controlled, in most instances, by the artificial rupture of the membranes combined with the subcutaneous administration of a minute amount of postpituitary. The resulting uterine activity presses the presenting vertex against the detached placental margin and uterine wall and thus controls bleeding.² The intravenous use of a solution of pituitary for placenta previa, a procedure suggested by Sachs, warrants severe criticism.

Post-partum Atony.—No dissenting voice has ever been raised against the invaluable aid rendered the obstetrician by the intravenous exhibition of postpituitary extract in the treatment of post-partum atony. The consensus of opinion prevails that this method which was advocated by the writer in 1918, has saved the life of the parturient woman on innumerable occasions. For the successful treatment of uterine atony post partum, the intravenous injection of a solution of pituitary deserves special consideration. "I believe it to be the greatest asset to the security of the doctor and the safety of his patient that has been given us in years" (Alden, Jackson). With this method, a dramatic, immediate and sustained response is obtained, the uterus contracting vigorously and remaining firm. For many years, I have followed the intravenous administration of postpituitary with neo-ergotamine, and I have never been obliged to pack the uterine cavity. The same method is employed after replacement of the inverted uterus.

REFERENCES

- (1) Hofbauer, J.: München. med. Wehnschr., p. 1210, 1912. (2) *Idem*: Monatschr. f. Geburtsh. u. Gynäk. 48: 325, 1918. (3) Newton, W. H.: J. Physiol. 89: 309, 1937. (4) Hofbauer, J.: J. Urol. 20: 413, 1928. (5) Reiman, E.: Med. Klin. 26: 960, 1930. (6) Jona, J. L., and Flecker, H.: Surg. Gynec. Obst. 51: 50, 1930. (7) DeLee, J. B.: Principles and Practice of Obstetrics, ed. 6, Philadelphia, W. B. Saunders Co. (8) Stoeckel, W.: Zentralbl. f. Gynäk. 60: 441, 1936. (9) Draper, W. B.: J. A. M. A. 1: 677, 1934. (10) Hofbauer, J.: Am. J. Obst. & Gynec. 26: 311, 1933. (11) *Idem*: Zentralbl. f. Gynäk. 61: 2482, 1937. (12) Alden, S.: New England J. Med. 209: 1211, 1933. (12a) Jackson: Discussion of Dr. Alden's paper. (13) Schoekaert, J. A.: Bruxelles-med. 17: 1091, 1937.

Editorial

The Dosage of the Estrogens

THE increasing employment of sex hormones in the treatment of gynecologic and other diseases calls for definite and accurate knowledge of the indications for their use and above all, of their dosage. While brilliant results are claimed for them as substitutes after operative or radiation treatment, much confusion has arisen from the many trade names under which estrogenic compounds are dispensed. Refinements in manufacture have made some of them available in crystalline form, synthetically produced, particularly the estrogens which are commonly known as estrone (theelin, ketohydroxyestrin, etc.) or estradiol (theelol, dihydroxyestrin, etc.).

Their satisfactory clinical application depends largely on proper and adequate dosage.

The estrogens, one of the two female sex hormones, the other being progesterone, the nidatory corpus luteum hormone, are now available in pure crystalline form. The estrogens are used clinically mainly in the form of estrone (theelin, ketohydroxyestrin) or estradiol (theelol, dihydroxyestrin). Confusion arises from the many trade names under which estrogenic compounds are disguised, amniotin, theelin, progynon-B and DH, ago and sistomensin, emmenin, menformon, to mention only a few. An international unit evaluating the potency of any given preparation of estrogens has been accepted. It is the effect produced by 0.1 *gamma* ($\frac{1}{10,000}$ of a gram) of estrone (theelin). This roughly corresponds to a mouse unit or $\frac{1}{5}$ to $\frac{1}{4}$ of a rat unit. For uniformity's sake all preparations should be standardized to the *international unit* (I.U.).

Some of the preparations are dispensed in water soluble, other in lipid soluble form. The rate of absorption, continuity of action and consequent physiologic effect produced is profoundly influenced both by the vehicle used and the site of injection.

Water soluble preparations are both more rapidly absorbed and excreted. Consequently more frequent injections and larger dosage is required. Oily solutions are taken up more slowly. The rate of absorption is more rapid from muscle than subcutaneous tissues. The disadvantage arising from repeated oil injections are the possible formation of painful, long persisting indurations or granulomas. Several preparations can be given by mouth. This is preferable to the patient but does not permit of as accurate dosage as by the parenteral route, because the amount of absorption through the intestinal tract varies in different individuals and under different conditions of food intake and intestinal function. Absorption of estrogens through the vaginal mucosa and through the skin likewise occurs. This method should not be used over long periods of time because carcinogenic potentialities are increased by topical application.

There are many pitfalls and variables to be considered, therefore the question of dosage always demands thought and consideration.

In the treatment of gonorrheal vaginitis of children as advised by Lewis¹ 1,000 I.U. by vaginal suppository are given daily until the discharge becomes acid and gonococci disappear (total dosage 30-50,000 I.U.).

In the treatment of the menopause marked divergence of opinion exists. In a series of cases controlled by hormone assay and vaginal spreads² an average of 150,000 I.U. per month were required. The estrogens were found equally effective whether given by injection or by mouth, although larger dosage is required. Werner³ obtained relief of symptoms with as little as 5,000 I.U. total (500 I.U. every third day for ten doses) injected in oily medium. All agree that repeated courses of treatment are required at intervals as the symptoms recur. Uterine bleeding may follow when medication is stopped. This form of treatment relieves not only the flushes and sweats but also psychical, arthritic, digestive and local vaginitic symptoms temporarily.

To produce bleeding in amenorrhea a much larger dosage is required.⁴ Bleeding may result from one million I.U.; frequently triple this amount is needed. The periodic return of menstruation by means of estrogens still remains a doubtful procedure, many careful observers having denied its success.

Estrogens have been used empirically for the treatment of numerous other conditions among which are hirsutes, toxemia of pregnancy, frigidity, sterility, dysmenorrhea, acne, etc. Theoretically such application appears illogical; the published reports are uncritical; no attempt to standardize dosage can be made for these conditions.

In prescribing and using estrogens the physician must select the preparation to be given according to the special requirements of the patient, keeping in mind the potency (I.U.), the vehicle, and the rate of absorption and excretion.

¹Lewis, R. M., and Adler, E. L.: *J. A. M. A.* 106: 2054, 1936.

²Frank, R. T., Goldberger, M. A., and Salmon, U. J.: *N. Y. State J. Med.* 39: 1363, 1936.

³Werner, A. A., Jones, G., Roberts, J., Brown, G. O., Neilson, C. H., and Rothermich, N. O.: *J. A. M. A.* 109: 1027, 1937.

⁴Frank, R. T., Goldberger, M. A., Salmon, U. J., and Felshin, G.: *J. A. M. A.* 109: 1863, 1937.

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF NOVEMBER 9, 1937

The following paper was presented:

A Contribution to the History of Obstetrics in New York City. Dr. Claude E. Heaton.

MEETING OF DECEMBER 14, 1937

The following papers were presented:

The Effect of Pregnancy on Women With Rheumatic Heart Disease. Dr. Burton K. Hamilton (by invitation).

Heart Disease Complicating Pregnancy. Dr. H. J. Stander. (For original article, see page 413.)

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF NOVEMBER 4, 1937

The following paper was presented:

Fetal Respiration in Relation to Atelectasis and Intrauterine Pneumonia. Drs. Franklin F. Snyder and M. Rosenfeld. (For original article, see page 363.)

MEETING OF DECEMBER 2, 1937

The following papers were presented:

The Prenatal Management of Breech Presentation. Dr. Jos. V. Missett.

The Management of Breech Deliveries. Dr. Roy W. Mohler. (For original article, see page 400.)

MEETING OF JANUARY 6, 1938

The following papers were presented:

A Case of Secondary Abdominal Pregnancy. Dr. C. W. Muckle. (For original article, see page 520.)

The Safety and Advantages of Office Currettage. Drs. S. Leon Israel and Charles Mazer. (For original article, see page 445.)

An Evaluation of the Sedimentation Test in the Differential Diagnosis of Acute Pelvic Inflammatory Disease and Acute Appendicitis. Drs. Charles Lintgen and Kenneth Fry. (For original article, see page 393.)

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF OCTOBER 22, 1937

The following paper was presented:

Inversion of the Uterus. Dr. Franklin E. Hall.

Hyperemesis Gravidarum. Drs. J. E. Fitzgerald and A. Webster. (For original article, see page 460.)

MEETING OF NOVEMBER 19, 1937

The following papers were presented:

Complications of Radiation Therapy in Cancer of the Cervix. Dr. Max Cutler.

Clinical Manifestation of Stricture of the Ureter in Women. Drs. E. L. Cornell and D. F. Rudnick.

MEETING OF DECEMBER 17, 1937

The following papers were presented:

Studies in the Evaluation of Mammography. Dr. Ralph A. Reis.

Infant Mortality at the Cook County Hospital Among 16,000 Deliveries. Drs. David S. Hillis and S. J. Benensohn. (By invitation.) (For original article, see page 427.)

The Pathologic Properties of Meconium. Drs. Wm. H. Rubovits, E. Taft (by invitation) and F. Neuwelt (by invitation). (For original article, see page 501.)

Effect of Placental Extract on Endometriosis. Dr. Mark T. Goldstine.

Atresia of the Vagina. Dr. Jos. L. Baer. (For original article, see page 518.)

BROOKLYN GYNECOLOGICAL SOCIETY*MEETING OF MARCH 4, 1938*

The following papers and case reports were presented:

Segmental Torsion of Fallopian Tube in a Young Virgin. Drs. Samuel A. Wolfe and David Kuperstein. (For original article, see page 509.)

Torsion of the Fallopian Tube. Dr. S. Kaminester. (For original article, see page 516.)

Primary Uterine Inertia. Dr. William S. Smith.

The Problem of Infant Mortality. Dr. Joshua Ronsheim. (For original article, see page 419.)

WASHINGTON GYNECOLOGICAL SOCIETY*MEETING OF JANUARY 23, 1937*

The following paper was presented:

The Use of Para Amino Benzene Sulphonamide or Its Derivatives in the Treatment of Beta Haemolytic Streptococcal Infections. Dr. Perrin H. Long and Eleanor A. Bliss.

MEETING OF MARCH 27, 1937

The following papers were presented:

Treatment of Gonorrheal Vulvovaginitis With Corbus-Ferry Filtrate. Dr. D. H. Kushner.

Diabetes Insipidus Complicated by Pregnancy. Dr. Herman Hertzberg.

Tumors of the Ovary. Dr. William Neill.

MEETING OF OCTOBER 23, 1937

The following papers were presented:

Neurotic Excoriations in Pregnancy. Dr. Edward M. Ellerson.

Impetigo Herpetiformis. Dr. I. Lewis Sandler.

OBSTETRICAL SOCIETY OF BOSTON*MEETING OF NOVEMBER 16, 1937*

The following paper was presented:

Obstetric Analgesia and Anesthesia. Dr. Charles P. Sheldon.

PITTSBURGH OBSTETRICAL AND GYNECOLOGICAL SOCIETY*MEETING OF FEBRUARY 7, 1938*

The following papers were presented:

Carcinoma of the Cervix During Pregnancy. Dr. Samuel Goldstein. (For original article, see page 514.)

Melanoma of the Vulva. Dr. R. C. Nucci. (For original article, see page 512.)

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

THE THYROID GLAND AND PREGNANCY*

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THE physiologic effect of pregnancy on the thyroid gland and the results of disorders of the thyroid gland on menstruation and the reproductive function have been the subject of considerable investigation and comment. This paper is a review of the more notable articles on these subjects which have appeared in the literature since about 1932. Mention is necessarily made of certain previous observations which clarify more recent statements.

There is an interrelationship of activity of the various endocrine glands. The function of the thyroid gland is the production of a secretion which activates heat and energy production by regulating the rate of oxidation in the cells throughout the body. The anterior lobe of the pituitary gland is the motor activator or dictator of activity of the endocrine glands but certain of its selective activities are held in check by at least some of these glands. For example, prolactin regulates the ovarian secretion of estrin and progesterin, but estrin in turn has an inhibitory action on the production of prolactin by the anterior lobe of the pituitary. Smith and others have demonstrated that removal of the pituitary glands of rats was followed by marked involution of the thyroid gland. These thyroid glands were restored to normal by the injection of fresh anterior pituitary substance. These and other experiments proved that the anterior lobe of the pituitary produces a secretion that stimulates and sustains the thyroid. This fraction of the secretion of the anterior pituitary lobe, the thyrotropic hormone, was isolated by Loeser in 1931 and by Anderson and Collip in 1933; the latter showed that this fraction acted on the thyroid and not on the sex glands. The thyrotropic hormone stimulates the activity of the thyroid cells to hyperplasia and the production of thyroxine and causes the release of stored colloid; too prolonged stimulation produces hyperthyroidism or thyrotoxicosis. Blum, however, observed that the metabolism stimulating effect of the daily administration of this thyrotropic hormone to rats and other animals was not sustained; after thirty to forty days the excessive rate of metabolism subsided, although the thyroid gland still showed hyperplasia. Later Collip and Anderson showed that the resistance to thyrotropic hormone was not due to a thyroid defense mechanism but to a substance circulating in the serum of the thyrotropic-resistant rat. Inasmuch as symptoms produced in animals

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by the thyrotropic hormone are strikingly similar to those of exophthalmic goiter in man, Marine speculated on the possibility that exophthalmic goiter occurs when the capacity to produce antihormone is impaired. Van Coubert and Stahl showed that thyroxin to a certain extent antagonizes the physiologic activity of the anterior lobe of the pituitary, and Kuschinsky demonstrated that the thyrotropic hormone content of the pituitary gland is inversely proportional to the thyroxin output of the thyroid gland.

For centuries it has been known that an increase in the size of the thyroid gland may occur during the menses and pregnancy and at the time of puberty and the menopause. Within comparatively recent years it has been noted that either hyperthyroidism or hypothyroidism may be accompanied by disturbances of menstruation, a decrease of fertility, and abortion. Marine stated that complete castration of dogs and rats is usually followed by a decrease in the size of the thyroid gland and a lowered rate of metabolism. Van Horn found that moderate thyroid feeding helps to eliminate estrin, although at the same time it stimulates the gonadotropic hormone of the anterior lobe of the pituitary to an increased production of estrin. Three times as much estrin was required to induce estrus in rats fed thyroid substance as in rats not so fed. It cannot be assumed, however, that these clinical observations or experimental findings are due to any selective action of the thyroid secretion on the ovaries or of the ovaries on the thyroid gland. In all probability the effects are produced through the anterior pituitary lobe, which acts as an intermediary. Evidence to support this belief is found in the temporary increase of gonadotropic and other activities of the pituitary gland following thyroidectomy and the decrease of thyrotropic as well as gonadotropic activity after injection of large doses of estrogenic substance. However, the work of Fluhmann suggests that thyroid substance inhibits the effect on the ovaries of the gonad-stimulating hormone of the anterior pituitary lobe and that this inhibition is the result of the direct effect on the ovary and not the result of indirect action through the anterior pituitary lobe.

Mention has been made that the secretion of the thyroid gland stimulates the body cells to produce energy and heat by regulating the rate of oxygen consumption. The normal average rate of metabolism of the body, calculated according to the DuBois standard, has been arbitrarily placed at zero, with normal variations between 10 per cent above and 10 per cent below this figure. The state of pregnancy demands increased secretion of the thyroid gland. Sandiford and Wheeler found that this was due to the increasing mass of active protoplasmic tissue, consisting largely of the fetal tissues and partly of an increase in maternal structures incident to pregnancy. These authors found that during the early months of pregnancy, there was little if any increase in the basal metabolic rate, but that there was a distinct increase to +20 or +25 per cent from the sixth month to the end of pregnancy. In 1931, Anselmino and Hoffmann demonstrated in the blood of pregnant women a substance which had the properties of thyroxin. This substance reached a maximal concentration at term and was found only in small amounts on the sixth day post partum. Mussey, Plummer and Boothby found that a basal metabolic rate of +25 or +30 per cent was not necessarily an indication of hyperthyroidism in the later months of pregnancy. Plass and Yoakam stated that the total increase of

metabolism due to the rapid rate of metabolic processes in the fetal tissues is about 15 per cent. They accepted the opinion of Benedict that the prediction standards of metabolism are 5 per cent too high for normal women and stated that any rate above +20 per cent was potentially abnormal. Bloss made basal metabolic tests a routine part of prenatal care and concluded that a rate of more than +20 per cent indicated a condition of hyperthyroidism. Hughes found a low rate in 77 per cent of women in the second, third, and fourth months of pregnancy and in 60 per cent up to the fifth month.

Women with a low basal metabolic rate and myxedema often have menstrual disturbances; they do not conceive. Women with a low basal metabolic rate without evidence of myxedema may suffer from severe menstrual disturbances, relative sterility, or abortion. Litzenberg and Carey noted that about a third of 137 women with a low basal metabolic rate had menstrual difficulties. These and other authors were able to avert abortion by administering thyroid extract to certain pregnant women with a low basal metabolic rate. Haines and Mussey reported a group of patients who had amenorrhea, oligomenorrhea, or menorrhagia and a low basal metabolic rate. These patients were treated only by means of desiccated thyroid in sufficient dosage to raise and maintain the basal metabolic rate at about -5 per cent. Definite improvement in the menstrual flow was obtained in 72 per cent of the cases of amenorrhea, in 55 per cent of those of oligomenorrhea, and in 73 per cent of those of menorrhagia.

Shute noted signs of mild hypothyroidism associated with an excess of estrin in the blood. He stated that the most sensitive diagnostic test for hypothyroidism is the reaction of the patient to thyroxin or thyroid extract. Patterson, Hunt and Nicodemus postulated that most thyroid disease is congenital. They concluded that: (1) the hypercholesteremia of pregnancy is due to a subclinical hypothyroidism that becomes exaggerated as the result of the increased metabolic demands of pregnancy, (2) the hypothyroid mother absorbs fetal thyroxin, producing fetal hypothyroidism from which the thyroid gland reacts to produce extreme fetal hyperplasia, and (3) the fetal thyroid hyperactivity and hyperplasia during development lead to permanent damage to the thyroid gland which, in later years and depending on the iodine supply and physiologic demands, may lead to clinically evident thyroid disease.

Carey and Brumfield, Randall, Titus, Bloss and others have successfully treated sterility among certain patients who had a low basal metabolic rate by the administration of sufficient thyroid extract to raise the rate to within normal limits. Hughes and Bloss noted an increased incidence of physical abnormalities among babies born to mothers who had hypothyroidism. The latter quoted Williams' *Obstetrics* to the effect that thyroid dysfunction results in a defective germ plasm and premature termination of pregnancy; if pregnancy continues, monstrosities result. Davis reported that low basal metabolic rates were common in the Milwaukee area and believed that a considerable number of children would have thyroid deficiency within a few years of birth if hypothyroid mothers did not receive thyroid medication during pregnancy. Bloss observed that most patients who suffered from nausea and vomiting had low basal metabolic rates and that relief was obtained upon administration of thyroid substance. This is at variance with the experience of Davis and of Falls, who noted that thyroid func-

tion is usually hyperactive in this condition. Our observations at the clinic would indicate that patients with hyperemesis may have either an increased or lowered basal metabolic rate, but this is only an occasional finding.

Many women with a basal metabolic rate below the average level do not have symptoms attributable to the hypothyroid state. When symptoms are produced by hypothyroidism, the rate of metabolism can be elevated carefully by the daily oral administration of thyroid extract. Mussey and Haines have advised giving a standard brand of desiccated thyroid in doses of about 4 gr. (0.24 gm.) daily for three or four days and then dropping the dose to from 1 or 2 gr. (0.065 or 0.12 gm.) daily. Determinations of the basal metabolic rate should be made every four to seven days in order to regulate the dosage. The optimal level of metabolism for these patients seems to be from -5 to -8 per cent. After the dose is regulated, determinations of the basal metabolic rate may be made at intervals of weeks or months. The most important observation made by those who have estimated the metabolic rate of many pregnant women may well be the apparent connection between maternal hypothyroidism and fetal anomalies. A pregnant woman with known hypothyroidism should be given enough thyroid extract to raise her metabolic rate to within normal limits. In many instances the metabolic rate will not show the usual rise during the third trimester of pregnancy. In fact we have noted symptoms of hyperthyroidism in a hypothyroid pregnant woman whose basal metabolic rate was elevated to +6 by the use of desiccated thyroid. In cases of hypothyroidism, Davis quite properly urged the institution early in pregnancy of thyroid medication; in fact, in recognized cases it should be begun prior to pregnancy in order that possible abortions or maldevelopments of the fetus may be avoided.

Mention has previously been made of the interrelationship of certain functions of the anterior lobe of the pituitary and of the thyroid and sex glands. The brief account of these functions has a bearing on recent new data concerning the relationship of these three glands during pregnancy. On the basis of this interrelationship Wiegand postulated an interesting theory of the etiology of eclampsia. Proof has been given of the presence in the blood of an antithyrotropic hormone. Wiegand stated that Herold had shown that, in the presence of increased thyroid function, such as in hyperthyroidism or during pregnancy, there is a decrease of antithyrotropic substances. After Eufinger and Anselmino and Hoffmann had found excessive function of the thyroid gland in eclampsia, Wiegand decided to examine the blood of healthy pregnant women and of women with eclampsia in order to determine, if possible, the relative presence of the antithyrotropic substance. After completing these examinations he stated that it was clear that the blood of women with eclampsia had a decreased amount of antithyrotropic substance and that this indicated in these patients an increased function of the thyroid gland which exceeded that of normal pregnancy.

In contrast with this evidence of hyperfunction of the thyroid gland it is of interest to note that Küstner reported administration of thyroxin in certain cases of eclampsia and pre-eclampsia associated with marked edema and albuminuria. Breipohl commented on the work of Küstner and cited the failure of response in similar cases in which patients were treated with thyroid under his supervision.

It has been stated previously that the thyrotropic hormone of the anterior pituitary lobe governs the normal function of the thyroid gland, which is the production of its internal secretion, thyroxin. The thyroid gland, however, requires iodine for the release of this secretion. In a special article on the physiology of the thyroid in 1935, Marine quoted the work of a number of investigators on the iodine content and requirements of the thyroid gland. Oswald showed that iodine in the gland was contained in colloid and he introduced the terms "thyroglobulin" and "iodothyroglobulin." Marine and Kimball demonstrated that the iodine store "in general varied inversely with the degree of active hyperplasia; in extreme degrees of thyroid hyperplasia the iodine store was exhausted. . . . The normal human thyroid weighs from 20 to 25 gm. and the maximum storage of iodine is from 20 to 25 mg., while the average normal total store is from 10 to 15 mg." They stated that part of the iodine fed to pregnant mothers is quickly stored in the fetal thyroid.

Marine reported that work hypertrophy or hyperplasia of the thyroid gland occurs when its iodine content falls below 0.1 per cent of its dried weight. C. H. Mayo and H. S. Plummer stated, "A supply of iodine inadequate for the proper functioning of the thyroid gland, followed by a subnormal delivery of thyroxin to the tissues, produces hypothyroidism; consequent elevation of intensity of thyroid stimulation causes diffuse hypertrophy of the thyroid gland; the secretory processes are altered; the diffuse hypertrophy disappears; colloid is stored in excess of the normal, and diffuse colloid goiter is the result."

So-called simple or colloid goiter, then, is the result of the deposit of colloid substance in the thyroid gland. This occurs when a functioning gland is not furnished with sufficient iodine to enable it to discharge all the thyroxin it is stimulated to produce. In other words, the deposit of colloid substance is not an indication of lowered thyroid function but rather of a deficient supply of available iodine. The amount of ingested iodine may be barely sufficient to supply the thyroid gland under ordinary conditions and quite insufficient for the extra physiologic demand of increased metabolism which occurs at puberty, during pregnancy, and sometimes during menses and at the menopause. Under such conditions this results in the commonly noted appearance of colloid or simple goiter. When the supply of iodine is particularly meager, as in parts of Switzerland and to a lesser extent in some regions of this and other countries, there is commonly an especially noticeable enlargement of the thyroid gland during pregnancy. When the supply of iodine remains low following confinement, this deposit of colloid material does not entirely subside and even shows an increase in size during subsequent pregnancies—Tait's so-called "step-ladder" enlargement noted by Gardiner-Hill.

In cases in which colloid goiter is present, the supply of thyroxin furnished by the gland may or may not be adequate to maintain a normal average metabolism in the individual. If it is not adequate a condition of hypothyroidism exists. If the mother has colloid goiter and an adequate amount of thyroxin is produced, the fetus will not develop colloid goiter providing there is sufficient iodine for the comparatively small demand of its normally functioning gland. If the mother has colloid goiter and an inadequate amount of thyroxin is produced, the fetus will have varying degrees of thyroid disturbance

depending on the degree of maternal hypothyroidism and the extent of failure of the iodine supply. The extent of the fetal thyroid disease will depend also on how greatly the lack of iodine may have previously affected the sperm cells or ovum or how much it affects the development and function of the fetal thyroid gland during embryonic development and throughout pregnancy. The fetal thyroid disturbance may vary from simple goiter with adequate glandular function to that total lack of thyroid development and function which is exhibited by the cretin. Mussey and Plummer have summarized the relationship of colloid goiter to pregnancy as follows: "The development of colloid or simple goiter during pregnancy may affect the future health of the mother, but it does not affect the normal progress of the pregnancy or the fetus unless the condition results in a sufficient degree of hypothyroidism to cause miscarriage or the development of colloid goiter or cretinism in the fetus."

The sources of iodine are the soil, ground water, and the sea. Sea fish have a relatively high content of iodine. The iodine content of leafy vegetables depends on the soil in which they were grown. In many regions where there is only a moderate lack of iodine, simple or colloid goiter does not become evident until the age of adolescence. Marine and Kimball and others have noted improvement or subsidence of the colloid or simple adolescent goiter following the administration of iodine. Davis and others reported that the use of small doses of iodine taken throughout pregnancy will prevent further enlargement of colloid goiter and even sometimes cause the gland to diminish in size. In regions in which colloid goiter is endemic, iodine may be supplied in the form of iodized salt which, according to Marine, should be in the proportion of one part of potassium iodide to 100,000 parts of salt. As a prophylactic for adolescents 10 mg. of iodine each week is commonly advised. Means advises one drop of compound solution of iodine (Lugol's solution) per week for adults.

Simple goiter needs no treatment except iodine during pregnancy. Frazier and Ulrich report the observations of 1,350 women who had simple goiter during early pregnancy. No complications developed as a result of the goiter and there was only one miscarriage in the group. Twelve patients underwent operation on the thyroid after delivery.

Mayo and Plummer and others have called attention to the development of new tissue, adenomatous goiter, which appears in many thyroid glands as the result of sustained stimulation in conjunction with certain unknown factors. The formation of adenomatous tissue is not common in the adolescent or more newly formed colloid goiter, but occurs with increasing frequency in women with colloid goiter as they grow older. In many of these cases, especially in the presence of large simple goiters, adenomatous nodules may be present in the gland and these may not be noticeable or may be difficult to detect. Although iodine is useful in the treatment of colloid goiter, observations indicate that the administration of preparations of iodine may cause the development of hyperthyroidism in cases of adenomatous goiter. It follows that preparations of iodine must be used with care in the treatment of adults who have large colloid goiters. For this reason Means, as previously mentioned, advised the use of one drop of compound solution of iodine per week for adults in goitrous regions.

Adenomatous nodules may occur in the thyroid gland without the presence of colloid. Many persons, mostly women, may have quiescent adenomas in the thyroid gland for many years. There is a tendency sooner or later, on the average seventeen years after the tumors are first observed, for such nodules to produce an excessive amount of thyroid secretion even though the function of the remaining portion of the gland is normal. This may occur during pregnancy, or more commonly the woman may become pregnant when the adenomas are hyperfunctioning. Mussey and Plummer reported that 50 per cent of the patients with adenomatous goiter and hyperthyroidism became worse during pregnancy, whereas in only 17 per cent of cases of exophthalmic goiter were the symptoms aggravated during pregnancy. Because of the tendency for the hyperthyroidism accompanying adenomatous goiter to become aggravated during pregnancy and because the benefits of iodine in the treatment of this condition are questionable, nearly all patients with hyperfunctioning adenomas are advised to have the adenomas removed unless such patients are within the last six weeks of pregnancy. Even then if the metabolic rate is over +50 per cent, if the hyperthyroidism has been maintained for a considerable period, if there is evidence of myocardial insufficiency, or if there is dyspnea caused by pressure of the adenoma on the trachea, it is usually safer to remove the adenoma prior to delivery of the baby. An example reported by Polowe is the case of a woman with acute hyperthyroidism of the adenomatous type who was in the third trimester of pregnancy. Medical measures failed and because of the aggravated symptoms, subtotal thyroidectomy was performed. The patient was delivered safely of a normal baby twelve days after estimated term and about two months postoperatively.

Neither hyperfunctioning (toxic) adenomas nor exophthalmic goiter is a common complication of pregnancy. Wallace reported 7 true and 2 doubtful cases of thyrotoxicosis complicating pregnancy among 11,571 obstetric patients at the Brooklyn Hospital, and Frazier and Ulrich reported 35 pregnant women with toxic goiter among 4,000 who had thyroid disease at the University Hospital in Philadelphia. Pregnancy may occur during a remission in the course of exophthalmic goiter or occasionally during a mild recurrence of exophthalmic goiter following subtotal thyroidectomy.

Exophthalmic, or so-called toxic, goiter is a more frequent complication of pregnancy than is hyperfunctioning adenoma. In a series of 83 cases of hyperthyroidism complicating pregnancy observed at the Mayo Clinic there were 57 cases of exophthalmic goiter and 26 cases of hyperfunctioning adenoma. Mussey and Plummer found that hyperthyroidism resulted in relative sterility, which was estimated to be about 25 per cent of normal fertility. Also, fully 90 per cent of our patients had symptoms of hyperthyroidism prior to conception. Bram found that 66 per cent of his patients had this syndrome when pregnancy began.

It is debatable whether the degree of hyperthyroidism is decreased or increased in the presence of pregnancy. Mussey, Plummer and Boothby found that pregnancy did not render the control of exophthalmic goiter more difficult. Wallace and Bothe agreed with this when they said that abortion was practically never indicated for hyperthyroidism. In mild cases abortion need not be considered. In severe cases the

strong possibility of a thyroid crisis or subsequent infection arising outweighs the benefits of abortion; also, abortion does not cure the disease.

Starr and Patton observed remissions in hyperthyroidism induced by the injection of an extract of pregnancy urine. They suggested that the excessive secretion of estrin suppressed activity of the anterior pituitary lobe, thus in turn lessening pituitary stimulation of the thyroid gland. Bodansky and Duff, and Danforth and Loumos, working independently, noted that pregnant rats tolerated doses of thyroid extract and thyroxin which in nonpregnant controls caused rapid loss of weight and death. More than the usual incidence of stillbirths occurred in rats so treated. These experiments suggested that hyperthyroidism, at least of a mild degree, might be tolerated better in the pregnant than in the nonpregnant state.

It has been stated that hyperthyroidism resulting from adenomatous goiter is not often controlled satisfactorily by iodine and that it is safer to remove the adenomatous goiter if this condition is present. It is generally agreed, however, that exophthalmic goiter is controlled at least temporarily by the administration of iodine. Mussey, Plummer and Boothby, Means, Bothe, and Bram and others have advised the use of iodine in the treatment of exophthalmic goiter during pregnancy. In mild cases the disease may be controlled until the natural termination of pregnancy. In mild cases in which the condition is not well controlled and in severe cases following temporary improvement, subtotal thyroidectomy is indicated. Bothe, however, stated that thyroidectomy was rarely necessary during pregnancy and Bram reported that 90 per cent of patients with hyperthyroidism can be carried to normal delivery. This does not, however, agree with the findings reported by Mussey and Plummer: of 29 patients with exophthalmic goiter, only 7 (24 per cent) were carried to term on medical management. This apparent difference in the management may be only relative, as comparatively few of the latter group could be classed as having mild hyperthyroidism.

I do not find in the recent literature mention of roentgen treatment for hyperthyroidism during pregnancy. However, since roentgen therapy has been employed for hyperthyroidism in nonpregnant patients, the following statement by Means is of interest: He stated that in a follow-up investigation after roentgen treatment of 44 patients with exophthalmic goiter and of 16 patients with toxic adenomas of the thyroid gland it was found that a third were cured, a third benefited, and a third obtained no benefit. Means said that he had abandoned roentgen treatment of hyperthyroidism since the introduction of iodine in the treatment of this condition.

In the treatment of hyperthyroidism complicating pregnancy, it may be well to consider the addition of vitamin B to the medication inasmuch as Means quoted Plummer (1926) and others (including Cowgill and Palmiere, 1933, Sure and Smith, 1934) who found that at a high level of metabolism more vitamin B is required to maintain body weight.

Mussey, Plummer and Boothby have reported that the administration of compound solution of iodine in doses of 10 drops three times a day in cases of exophthalmic goiter is ordinarily followed by distinct improvement and by a definitely lowered basal metabolic rate within two weeks.

In the occasional case of exophthalmic goiter, within two weeks after the use of iodine a remission may follow which is complete or nearly complete, the basal metabolic rate being approximately normal or within normal limits for the period of pregnancy. In certain cases of such rapid and marked remission the patient may be carried through pregnancy by the administration of iodine. These patients must be observed carefully, however, and the basal metabolic rate must be determined occasionally as recrudescence of the disease often occurs in spite of the continued use of iodine. Except in certain cases in the last trimester of pregnancy, partial thyroidectomy should be performed without delay if the exophthalmic goiter does not show complete or nearly complete remission within two weeks after treatment with iodine is begun. A false sense of security may lead to the operation being deferred to a less favorable period of pregnancy or to a time when iodine may fail to give as complete protection against postoperative reaction, or irreparable damage to vital organs may occur. There may be exceptions to this rule in cases in which complicating conditions other than normal pregnancy exist. Whether or not operation is performed in cases of exophthalmic goiter or hyperfunctioning adenomas, aside from the judicious use of iodine the treatment is the same as that usually given to women during pregnancy and confinement.

Means has written the following concise, clear summary of the management of hyperthyroidism complicating pregnancy: "Women with toxic goiter may become pregnant, or pregnant women may become thyrotoxic. In either event it is the thyrotoxicosis, not the pregnancy, which should be interrupted. If the thyrotoxicosis is not interrupted, it often causes the interruption of the pregnancy. A pregnant woman with toxic goiter can be put through the usual routine treatment, subtotal thyroidectomy after iodination, without aborting, and proceed to go to full term normally.

"The physician is often asked whether previous toxic goiter makes pregnancy undesirable. We have seen no reason to suppose that it does. If the thyrotoxicosis has been cured there is no reason to suppose that a woman will come to any harm attributable to her past thyroid disease if she becomes pregnant. We have had a number of patients that have done so and all has gone smoothly with them. On the other hand, if there is any element at all of persistent or residual thyrotoxicosis pregnancy is undoubtedly contraindicated. It is wise to advise that a pregnancy be not undertaken until two years after the ending of the toxic goiter."

REFERENCES

- (1) *Anderson, E. M., and Collip, J. B.*: Proc. Soc. Exper. Biol. & Med. **30**: 680, 1933.
- (2) *Anselmino, K. J., and Hoffmann, Friedrich*: Arch. f. Gynäk. **145**: 95, 1931.
- (3) *Benedict*: Quoted by Plass, E. D., and Yoakam, W. A.
- (4) *Bloss, J. R.*: South. M. J. **30**: 637, 1937.
- (5) *Blum, F.*: Schweiz. med. Wehnschr. **63**: 777, 1933.
- (6) *Bodansky, M., and Duff, Virginia B.*: Endocrinology **20**: 537, 1936.
- (7) *Bothe, F. A.*: Ann. Surg. **101**: 422, 1935.
- (8) *Bram, Israel*: Pennsylvania M. J. **39**: 239, 1936.
- (9) *Breipohl, Wilhelm*: Klin. Wehnschr. **15**: 1203, 1936.
- (10) *Carey, J. B., and Brumfield, Helene P.*: Minnesota Med. **16**: 396, 1933.
- (11) *Collip, J. B., and Anderson, Evelyn M.*: Lancet **1**: 76, 1934.
- (12) *Cowgill and Palmiere*: Quoted by Means, J. H.
- (13) *Danforth, D. N., and Loumos, S.*: Proc. Soc. Exper. Biol. & Med. **34**: 870, 1936.
- (14) *Davis, C. H.*: AM. J. OBST. & GYNEC. **30**: 570, 1935.
- (15) *Eufinger*: Quoted by Wiegand, Max.
- (16) *Falls, F. H.*: Northwest Med. **28**: 391, 1929.
- (17) *Fluhmann, C. F.*: Am. J. Physiol. **108**: 498, 1934.
- (18) *Frazier, C. H., and Ulrich, H. F.*: AM. J. OBST. & GYNEC. **24**: 870, 1932.
- (19) *Gardiner-Hill, H.*: Lancet **1**: 120, 1929.
- (20) *Haines, S. F.*,

- and Mussey, R. D.: J. A. M. A. 105: 557, 1935. (21) Herold: Quoted by Wiegand, Max. (22) Hughes, E. C.: New York State J. Med. 34: 873, 1934. (23) Kuschinsky: Quoted by Means, J. H. (24) Küstner: Quoted by Breipohl, Wilhelm. (25) Litzenberg, J. C., and Carey, J. B.: AM. J. OBST. & GYNEC. 17: 550, 1929. (26) Loeser, Arnold: Arch. f. exper. Path. u. Pharmacol. 163: 530, 1931. (27) Marine, David: J. A. M. A. 104: 2250, 1935. (28) Marine, David, and Kimball, O. P.: J. A. M. A. 77: 1068, 1921. (29) Mayo, C. H., and Plummer, H. S.: The Thyroid Gland, St. Louis, 1926, The C. V. Mosby Company, 83 pp. (30) Means, J. H.: The Thyroid and Its Diseases, Philadelphia, 1937, J. B. Lippincott Company, 602 pp. (31) Mussey, R. D., and Haines, S. F.: AM. J. OBST. & GYNEC. 27: 404, 1934. (32) Mussey, R. D., and Plummer, W. A.: J. A. M. A. 97: 602, 1931. (33) Mussey, R. D., Plummer, W. A., and Boothby, W. M.: J. A. M. A. 87: 1009, 1926. (34) Oswald, A.: Quoted by Marine, David. (35) Patterson, W. B., Hunt, H. F., and Nicodemus, R. E.: West. J. Surg. Obst. & Gynec. 45: 486, 1937. (36) Plass, E. D., and Yoakam, W. A.: AM. J. OBST. & GYNEC. 18: 556, 1929. (37) Polowe, David: J. A. M. A. 99: 2180, 1932. (38) Randall, L. M.: Personal communication to the author. (39) Sandiford, Irene, and Wheeler, Theodora: J. Biol. Chem. 62: 329, 1924. (40) Shute, Evan: Canad. M. A. J. 35: 622, 1936. (41) Smith, P. E.: Am. J. Anat. 45: 205, 1930. (42) Starr, Paul, and Patton, Helen: Ann. Int. Med. 8: 825, 1935. (43) Sure and Smith: Quoted by Means, J. H. (44) Tait: Quoted by Gardiner-Hill, H. (45) Titus, Paul: South. M. J. 30: 410, 1937. (46) Van Coubert and Stahl: Quoted by Means, J. H. (47) Van Horn, W. M.: Endocrinology 17: 152, 1933. (48) Wallace, J. T.: AM. J. OBST. & GYNEC. 26: 77, 1933. (49) Wiegand, Max: Arch. f. Gynäk. 163: 138, 1936. (50) Williams: Quoted by Bloss, J. R.

Erratum

June 15, 1938.

Dear Dr. Kosmak:

I neglected to emphasize a point about distilled water that should have been made in the article on estrogen assay in the blood in the June issue of the THE AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY. It is too important to pass without mention, however.

The pH of the distilled water should not be below 6.4 and the titrable acidity per liter should not exceed 20 c.e. of N/100 HCl using phenolphthalein. Ordinary laboratory distilled water usually meets such requirements. But if the acidity should be higher the difficulty may be overcome by boiling for a few minutes, allowing to cool in a stoppered container, and using while fresh.

(Signed) E. V. Shute.

London, Ontario

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Puerperium

Rivière and Legrosdidier: Azotemia and Polypeptidemia in the Puerperium, *Gynéc. et obst.* 35: 437, 1937.

This study represents a continuation of Estienny's original work and records their own subsequent researches on post-partum blood nitrogen values. In a small series of 20 normal patients, of whom 19 were delivered spontaneously and 3 by forceps under chloroform anesthesia, blood samples were taken several hours post partum, and on the sixth and twelfth days.

Puerperal elevation of blood nitrogen is physiologic and affects both urea and the polypeptids. The latter increase to a much higher level than do the former, reaching a maximum about the sixth day; both the rise and the decline of the polypeptids precede that of the urea. In the three patients submitted to chloroform anesthesia, the highest polypeptid values occurred.

The authors state that it is possible though not certain that the elevated puerperal blood nitrogen may be a humoral reflection of uterine involution. However, since the polypeptids in 50 per cent of cases become maximal within the immediate post-partum hours when the processes of involution can hardly have begun, this is not very likely. They do not believe that high puerperal polypeptid values are responsible for obstetric shock or post-partum eclampsia.

ARNOLD GOLDBERGER.

Hemmings, C. T.: A Study of Post Delivery Deaths Caused by Embolism, *Ohio State M. J.* 32: 620, 1936.

The total incidence of post delivery embolism in a series of 80,136 births studied by Hemmings was 0.04 per cent. Post delivery embolism in this study presented an incidence of 7.8 per cent of the total deaths and 14.5 per cent of the delivery deaths. The incidence of post delivery embolism was more than three times greater where operative interference was used than in normal deliveries. Cesarean section rated second in incidence of all operative procedures. Adequate prenatal care did not prevent embolism. The most outstanding causative factors in this review were hemorrhage, trauma, infection, and venous stasis. Available blood counts generally revealed a well-marked secondary anemia. Symptoms of phlebitis were present in only 24.3 per cent of the patients. Medication used had no direct bearing on the causation of embolism.

The causative factors can be prevented by: (1) A more thorough prenatal study of obesity, hypotension, anemia, and toxemia. (2) The development of better aseptic technic to prevent infection. (3) The reduction of operative interference to reduce trauma. (4) The reduction of blood loss during labor and delivery. (5) More liberal employment of blood transfusions. (6) Routine leg exercises to combat circulatory stasis.

J. P. GREENHILL.

Williams, J. T.: Epidemic Puerperal Sepsis, New England J. Med. 215: 1022, 1936.

According to Williams, puerperal infections may be divided into simple wound infections and epidemic puerperal infections usually due to *Streptococcus hemolyticus*. Operative vaginal delivery and, more especially, cesarean section greatly increase the incidence of all types of infection. Mortality is practically the same for operative and nonoperative deliveries, but much higher after cesarean section. Ordinary, or even extraordinary, aseptic precautions are not sufficient to guard against the epidemic type of infection.

No treatment, except possibly transfusion of immune blood, is of any value in epidemic *Streptococcus hemolyticus* infections. Immediate isolation of all patients showing symptoms suggestive of severe puerperal infection is the chief means of preventing development of epidemics. Culturing the throats of the staff, interns and nurses is not of much value unless the hospital has bacteriologic facilities for typing the streptococci that are found. Careful masking of all delivery room attendants is essential, although it is admitted that most of the present-day masks are inefficient.

J. P. GREENHILL.

Bonney, Victor: Puerperal Sepsis From the Viewpoint of Surgery, Brit. M. J. 1: 295, 1936.

The author contrasts the sources of infection in surgery as compared with spontaneous labor. He believes most puerperal sepsis is extrinsic and occurs after delivery. In England, for every 1,000 children born alive about two mothers die of puerperal sepsis.

The sepsis morbidity rate is 1 per cent. This is a low standard as compared to that of surgery. In a certain proportion of sporadic cases of puerperal sepsis, the infection is from an intrinsic source; "spray infection" is not the only source of puerperal infection. Extrinsic infection can readily be conquered; intrinsic sources provide more obstacles and only by adopting complete surgical methods can their menace be met. These methods consist of thorough sterilization of the approaches to the operation area, the avoidance of undue trauma, and hemorrhage in that area, and removal beforehand of septic foci of infection in other parts of the body.

The near future may provide reliable immunization prior to operation. The obstetrician should approach his cases with the same attitude that the surgeon assumes when attending an operation or taking part in it.

F. L. ADAIR AND S. A. PEARL.

Rose, J. K.: Hemolytic Streptococcal Puerperal Infection, J. Obst. & Gynaec. Brit. Emp. 44: 278, 1937.

Observations on incidence of hemolytic streptococci in lying-in women have been made by the author over a period of six years. Coordination of clinical and laboratory work insures that the presence of pathogenic organisms in patients or staff is known at the earliest possible moment and allows for more speedy and accurate diagnosis of the cause of minor symptoms and rise of temperature. In routine examination of nurses admitted for training it is found that a few in each group harbor organisms which may be a source of danger. When definite foci exist, appropriate treatment has proved effective.

In hospital patients the probable infective factors were: autoinfection in one; autoinfection and complicated labor in four; difficult labor in two; infected attendant and complicated labor in two; and infected attendant one case. In district work the most important factor appeared to be infection in the patient or her relatives, frequently associated with anemia and general debility, the result of unsatisfactory social conditions.

Prophylactic measures should include: (1) Effective treatment of infections of throat and nose in those who undertake midwifery; (2) isolation in hospitals to protect the clean patients from any who are potential sources of infection; (3) prenatal treatment of the potentially infected patient if obstetric operation is anticipated; (4) early postnatal treatment of the infected patient before symptoms develop; (5) immediate investigation of contacts if swabs taken early in the puerperium show that a patient who was previously negative has acquired a new infection.

J. P. GREENHILL.

Burton, A. H. G., and Weir, J. H.: Puerperal Surgical Scarlet Fever, Lancet 1: 1110, 1936.

The authors give a condensed review of the subject and quote C. C. Okell on two modes of infection. The first is the ordinary scarlet fever due to a primary faucial infection, while the second is due to a primary infection of the uterus. It is recommended that the second class be regarded as a "surgical scarlet fever with the local lesion in the genital tract." From the focus of a streptococcal endometritis or a streptococcal cervicitis toxins are liberated into the general circulation and thus produce the characteristic picture of scarlatina. Locally the streptococcus produces the usual effects of a puerperal sepsis.

In the three cases reported each developed the typical syndrome of scarlet fever "including a well-marked faucial lesion, strawberry tongue, and brilliant rash followed by wide-spread desquamation." Cultures from the throat were negative for hemolytic streptococci, while those from the cervix were positive. These organisms were all inagglutinable with the ordinary scarlet fever type sera. Although all three patients were attended by the same physician, his nose and throat cultures were negative for hemolytic streptococci. Other measures to determine a possible source were not mentioned. Serotherapy gave good results and was followed by no serious complications.

In view of the authors' apparent good results with the scarlatinal antitoxin in three cases, they recommend that this therapeutic agent be further studied before condemning it as other investigators with much larger series have urged.

H. CLOSE HESSELTINE.

Wood, J. L. Miller: Puerperal Infections in Relation to Midwifery Attendants, Brit. M. J. 2: 811, 1937.

The bulk of serious cases of puerperal infection are due to infection with *Streptococcus pyogenes* Group A. These organisms are frequently carried by attendants and midwives. In order to demonstrate the identity of the organism swabs should be made from the cervix and throat of the patient, as well as blood cultures. Until the results are known, the midwife should cease to attend any further cases. Swabs from the noses and throats of contacts and midwife should be made. If positive for *Strep. pyogenes*, it should be typed in order to identify it and demonstrate the true source of the infection.

Midwives should be suspended from duty if they have a cold or tonsillitis or have been in attendance upon a case of scarlet fever. Bacteriologic studies if negative will permit the midwife or nurse to resume duties. The prospect of obtaining a swab-negative state from a suspended midwife or attendant is not so gloomy as might be imagined.

It appears essential in the interests of patient and attendants that all cases of pyrexia during the puerperium be investigated. The swabbing of clinically normal throats, unless they are believed to be a source of infection, cannot be too much deprecated.

F. L. ADAIR AND S. A. PEARL.

Snoeck, J., and Rocmans, M.: Influence of the Retention of the Membranes on Puerperal Morbidity, Rev. franç. de gynéc. et d'obst. 32: 504, 1937.

The authors found that the total morbidity during the puerperium is the same after normal complete labors as it is following deliveries in which parts of the membranes are retained in the uterus. They believe that invasion of the uterus is useful only when there is persistence of abnormal bleeding which might indicate the possibility of retention of a portion of placenta. Exploration of the uterus for partial retention of the membranes does not ameliorate the state of the puerperium either as regards temperature or late hemorrhages.

J. P. GREENHILL.

Aisenberg-Qulianitzkaia, E. M.: The Treatment of Puerperal Septicemia by Intravenous Injections of Alcohol, Rev. franç. de gynéc. d'obst. 31: 777, 1936.

During the past year and a half the author observed 24 cases of puerperal septicemia, nine of which followed labor and 15 occurred after abortion. Blood transfusions were employed in 6 cases but intravenous injections of alcohol were given in all the cases. Seventeen women recovered and 7 died, giving a mortality of 37.5 per cent. The author considers this death rate a triumph for the use of alcohol and recommends this form of therapy for all cases of septicemia. He cannot explain the beneficial action of the alcohol in these cases, but it does stimulate the body activities, it supplies nourishment, it stimulates diuresis, sleep, and the appetite. The addition of glucose to the alcohol is desirable because it reinforces the action of the alcohol. The author believes that alcohol injections may also prove beneficial in cases of infectious diseases.

J. P. GREENHILL.

Livingston, Seymour H., and Blum, Samuel G.: Prophylactic Use of Ergot and Ergotamine Tartrate in Puerperium, Am. J. Surg. 31: 533, 1936.

On the basis of this study of 506 post-partum cases, the authors are unable to agree with other investigators who have reported marked acceleration of involution by the prophylactic use of ergotamine. However, they find that it does give a distinct reduction in the incidence of foul lochia and morbidity. Fluidextract of ergot (U. S. P.) also seems to be of some value in this respect if given intensively for a short period of time. There seems to be a somewhat more marked prophylactic effect following the use of ergotamine.

J. THORNWELL WITHERSPOON.

Voron, Pigeaud, and Burtheault: Attempt at Prophylaxis of Puerperal Infection by Means of "benzyl-amino-benzene-sulfamide," Bull. Soc. d'obst. et de gynéc. 26: 734, 1937.

For the past several years, in the Lyon Obstetrical Clinic, benzyl-amino-benzene-sulfamide was administered to a series of obstetric patients on the evening they were delivered, the day following, and also on the third day. In a series of 537 patients who received this prophylactic treatment the incidence of morbidity following delivery was 9 per cent. In a control group of 556 women who did not receive any prophylactic medication, the incidence of morbidity was 11.3 per cent. One patient died of puerperal infection though she had received prophylactic treatment. The authors admit that these results are not conclusive.

J. P. GREENHILL.

Leon, Juan, and Ferrari, Roberto A.: Preventive Chemotherapy of Puerperal Infection, Bol. Soc. obst. y ginec. de Buenos Aires 16: 300, 1937.

Sulfanilamide was administered to every patient admitted to the clinic and for four to five days post partum. In cases of ruptured membranes, immediately upon

this happening, and to women admitted in labor, sulfanilamide was also given. The dose used was prontosil soluble 5 c.c. of a 2.5 per cent solution; other derivatives were employed in about the same dose.

The series consists of 9 women with premature rupture of membranes, 289 women admitted during labor and 69 immediately following labor.

Intolerance to the drug was not very often seen nor was it severe. Some patients developed a slight digestive disturbance, some had slight decrease of appetite, one woman had a skin eruption. There were no changes noted in the blood or urine, but the drug was not administered to women with kidney or liver damage.

The authors feel that, in the cases studied by them, prophylactic use of sulfanilamide justified itself although further study must be made on surgical and apparently infected cases.

MARIO A. CASTALLO.

Foulis, M. A.: Prontosil Album in Puerperal Sepsis, Brit. M. J. 1: 445, 1937.

The author reports on the favorable use of prontosil tablets in puerperal sepsis. In a series of 70 such cases 22 received oral therapy. Four patients had additional prontosil soluble injections.

Of the orally treated cases 11 had septicemia; 8 had positive hemolytic streptococci in blood cultures; 3 cases of peritonitis without septicemia had hemolytic streptococci in the peritoneal fluid cultures; the remaining 7 had hemolytic streptococci in the vaginal discharge.

The dose used was high, ranging from 3 gm. (10 tablets) to 14.4 gm. every twenty-four hours at four-hour intervals. The drug was well tolerated. Toxic effects were minimal. The fall in temperature and the general improvement were rapid and striking. The mortality rate in this group was 1.4 per cent (one death) compared with 13.4 per cent in a five-year period in the same hospital.

F. L. ADAIR AND S. A. PEARL.

Drew-Smythe, H. J.: Prontosil in Obstetrics, Bristol Med.-Chir. J. 54: 217, 1937.

In spite of the possible complications that may arise from its prolonged use, prontosil and its derivatives offer a most potent agent in the prevention of morbidity and mortality associated with puerperal sepsis. The drug is not specific in its action against streptococci. Good results have been reported in cases of *Bacillus coli* pyelitis and in staphylococcal infections. Its action is obviously not that of a bactericide, but it evidently renders the infecting organisms more susceptible to attack by the natural defense forces.

The author reports a typical case of puerperal infection in which the drug was used successfully. The question of sulphemoglobinemia is discussed. Mild degrees of psychosis have followed the use of the drug.

F. L. ADAIR AND S. A. PEARL.

Colebrook and Purdie: Treatment of 106 Cases of Puerperal Fever by Sulphanilamide, Lancet 2: 1237, 1937.

The authors report the results of treatment with sulfanilamide (para-amino-benzene sulfonamide) in puerperal infection and compare the results with those previously obtained with sulfamido-chrysoidine (red prontosil) and prontosil soluble and also with the cases treated from 1931 to 1935 when no specific treatment was used.

One hundred cases of puerperal infection due to hemolytic streptococci (92 of Lancefield Group A), 3 due to anaerobic streptococci, and 3 due to staphylococci were treated with sulfanilamide. The results are similar to those reported previously in 64 patients treated with red prontosil and prontosil soluble but a little less spectacular. Eight deaths occurred in the 100 cases. The mortality rate for the

199 cases infected by hemolytic streptococci treated since these drugs were first used (1936) has been 5.5 per cent as compared with 22.8 per cent for the preceding five years.

Cyanosis developed in 58 of the 100 cases and was usually associated with met- and sulphhemoglobinemia. "Drug fever" was suspected in several instances. Prostration, paraesthesia, headache, visual disturbances, and joint pains also occurred. No generalized rashes developed.

The dosage suggested is relatively large, 8 to 15 gr. daily for the first few days in the severe infections. It should be reduced if there appears to be any adverse effect and in any case as soon as definite clinical improvement is seen.

CARL P. HUBER.

Gibberd, G. F.: Prontosil and Similar Compounds in the Treatment of Puerperal Haemolytic Streptococcus Infections, Brit. M. J. 2: 695, 1937.

The author compares the results of 1936 and 1937, when the new aniline chemotherapy was used in puerperal sepsis due to hemolytic streptococci, with those obtained in the 1934 and 1935 period. It is apparent that since the introduction of prontosil and prontosil there has been a marked improvement in the results. This is demonstrated by: (1) a fall in total mortality rate; (2) a reduction in the proportion of cases in which the infection spread beyond the limits of the birth canal, and by the relative infrequency with which an inflammatory mass developed after treatment had been instituted; (3) a significant fall in the mortality rate in cases of proved septicemia associated with a relative decrease in the proportion of severe cases of septicemia and by a fall in the incidence of septicemia developing after the treatment had been instituted; and (4) by the relative infrequency with which generalized peritonitis has been found post mortem.

These results can scarcely be explained by an assumption that the virulence of the hemolytic organism had diminished spontaneously in that period.

F. L. ADAIR AND S. A. PEARL.

Item

American Board of Obstetrics and Gynecology

The next written examination and review of case histories of Group B applicants by the American Board of Obstetrics and Gynecology, will be held in various cities of the United States and Canada on Saturday, November 5, 1938. Last day for applying is September 5.

The next general examination for all candidates (Groups A and B) will be held in St. Louis, Missouri, in June, 1939, immediately prior to the American Medical Association meeting.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania. Applications for these examinations must be filed in the Secretary's Office not later than sixty days prior to the scheduled dates of examination.